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CARCINOGENESIS ABSTRACTS

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CARCINOGENESIS ABSTRACTS

VOLUME 15, ISSUE 7

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GENERAL INFORMATION

CARCINOGENESIS ABSTRACTS makes available abstracts, annotations or citations of significant carcinogenesis articles collected from the current major biomedical sources of world literature. This service is provided by the National Cancer Institute through a contract with The Franklin Institute Research Laboratories for preparation of the publication, under Contract No. NOI-CP-75885 with the National Cancer Institute, U.S. Department of Health, Education and Welfare. Published and distributed by The Franklin Institute Press^{SM}.

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ABBREVIATIONS

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LANGUAGE of the article is indicated in parentheses after the title and is represented by a three-letter code. The source for these codes is *MARC Manuals Used by the Library of Congress,* pages 183-187.

ABBREVIATIONS used in abstracts:

A	angstrom(s)
ACTH	adrenocorticotropic hormone
ADP	adenosine diphosphate
AMP	adenosine monophosphate
ATP	adenosine triphosphate
approx	approximately
av	average
BCG	bacillus Calmette-Guerin
bid	twice daily
C	degree(s) centigrade
cal	calorie(s)
kcal	kilocalorie(s)
cc	cubic centimeter(s)
Ci	curie(s)
mCi	millicurie(s)
μCi	microcurie(s)
cm	centimeter(s)
CNS	central nervous system
cpm	counts per minute
DNA	deoxyribonucleic acid
ED$_{50}$	median effective dose
EDTA	ethylenediamine tetraacetic acid
g	gram(s)
kg	kilogram(s)
mg	milligram(s)
μg	microgram(s)
Hb	hemoglobin
hr	hour(s)
ia	intra-arterial
id	intradermal
IgA	Immunoglobulin A
IgB	Immunoglobulin B
IgG	Immunoglobulin G
IgM	Immunoglobulin M
ILS	increased life span
im	intramuscular
ip	intraperitoneal
IU	International Unit(s)
iv	intravenous
Km	Michaelis constant
LD	lethal dose
LD$_{50}$	median lethal dose
M	molar
μM	micromolar
mOsm	milliosmolar
max	maximum
mEq	milliequivalent(s)
min	minute(s)
ml	milliliter(s)
μl	microliter(s)
mm	millimeter(s)
mo	month(s)
mol wt	molecular weight
N	normal concentration
NAD	nicotinamide adenine dinucleotide
NADH	reduced nicotinamide adenine dinucleotide
NADP	nicotinamide adenine dinucleotidephosphate
NADPH	reduced nicotinamide adenine dinucleotidephosphate
NCI	National Cancer Institute
NIH	National Institutes of Health
PAS	periodic acid-Schiff
po	orally
ppb	parts per billion
ppm	parts per million
qid	four times daily
qod	every other day
QO$_2$	oxygen quotient
R	roentgen
RBC	red blood cells (erythrocytes)
RNA	ribonucleic acid
rpm	revolutions per minute
sc	subcutaneous
sec	second(s)
SGOT	serum glutamic-oxaloacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
soln	solution
TCD	tissue culture dose
TCD$_{50}$	median tissue culture dose
tid	three times daily
UV	ultraviolet
WBC	white blood cells (leukocytes)
wk	week(s)
wt	weight
X	times
yr	year(s)

77-3601 **Carcinogenesis and Tumor Growth.** (Eng.) Hill, H. Z. (Dept. Biochemistry, Marshall Univ. Sch. Medicine, Huntington, WV) Lin, H. S. *In: Clinical Oncology.* Horton, J.; Hill, G. J., eds. (Philadelphia: W. B. Saunders Co.) pp. 1-33; 1977.

Tabulated data on the relative percentage of incidence of (1955-1964) and mortality from (1974) cancer by site and sex in the US and on estimated new cases and deaths by site and sex for 1976 is presented. Reverse transcriptase (RT) has been discovered in a number of cancer cells of several animals and man. The presence of RT in a tumor is often taken as clear-cut evidence of a viral etiology. RNA C-type viruses have been found in human cells after long-term culture, and, recently, C-type viral antigens were found in WBC of five patients with acute leukemia. These antigens cross-reacted with those from C-type viruses from a woolly monkey and a gibbon ape. B-type RNA viruses, or mouse mammary tumor viruses, are present in the milk of certain strains of mice. RNA viruses might also be involved in the induction of human breast cancer. Herpesviruses are the most likely of the DNA viruses to produce cancer in humans. Environmental carcinogens, such as benzo(a)pyrene, asbestos, and vinyl chloride, and physical carcinogens, such as irritation, trauma, radiation, and radionuclides, and their proposed mechanisms of action are reviewed. Cellular transformation, cancer genetics (mutation theory, inheritance factor, chromosomal aberrations, gene action), tumor progression (immune surveillance, influence of sex hormones and chalones, differentiation, stem line evolution, biochemical factors), and tumor cell population kinetics are also surveyed. (164 refs.)

77-3602 **Carcinogenesis, 1957-77: Notes for a Historical Review.** (Eng.) Saffiotti, U. (Experimental Pathology Branch, Carcinogenesis Program, Div. Cancer Cause and Prevention, NCI, NIH, Bethesda, MD 20014) *J Natl Cancer Inst* 59(2, Suppl): 617-622; 1977.

The scientific bases, research and documentation methodologies, and ethical principles used to identify the chemical and physical causes of cancers and the means for their prevention that have been established over the last 20 yr are reviewed. Scientific advances and role of the National Cancer Institute are discussed in detail. (33 refs.)

77-3603 **Proposal: A Non-zero Approach to Environmental Limits for Carcinogens.** (Eng.) Flowers, E. S. (Div. Criteria Documentation, Natl. Inst. Occupational Safety and Health, Rockville, MD) *Occup Health Saf* 46(3): 35-39; 1977.

It is suggested that acceptable environmental levels of chemical mutagens and carcinogens can be estimated by calculating the radiation-equivalent chemical (rec) dose that would result in a risk of cancer at a particular site equivalent to the risk from background radiation sources (0.49 milliroentgen-equivalent-man/day). Calculated rec limits for $>$ 20 agents are quoted; eg, for 2-acetylaminofluorene with the whole body as a "target organ", the estimated atmospheric rec limit is 0.1 ppb; for benzidine with the bladder as a target organ, the estimated rec limit is 0.01 ppb; for asbestos with the lungs as a target organ, the estimated rec limit is 3 fibers/ml. Mechanisms of carcinogenesis and tumor proliferation are also discussed. (31 refs.)

77-3604 **General Criteria for Assessing the Evidence for Carcinogenicity of Chemical Substances: Report of the Subcommittee on Environmental Carcinogenesis, National Cancer Advisory Board.** (Eng.) Shubik, P. (Office Cancer Communications, NIH, Building 31, Room 10A17, Bethesda, MD 20014) *J Natl Cancer Inst* 58(2): 461-465; 1977.

Criteria to be used as guidelines in assessing the value of carcinogenicity data are presented. Three sources of data are recognized and discussed: (1) human studies, (2) animal studies (bioassays), and (3) in vitro tests. Some animal studies may require additional confirmation before they can be extrapolated to the particular conditions of human exposure. These studies include (1) bioassays employing inbred strains of animals that develop high incidences of particular tumors in the untreated state; (2) bioassays in which, in addition to the test agent, animals are treated with a known carcinogen or some other foreign material that itself may be carcinogenic or cocarcinogenic; (3) bioassays in which the test animals are subjected to grossly unphysiologic and inappropriate conditions; and (4) bioassays in which the test compound is given by unusual routes of administration (such as bladder implantation), and there is reason to believe that the resulting tumors may not be due to a specific effect of the test compound. Regarding the uncertain extrapolation from animal studies, it is stated that: "Each case must be individually evaluated, taking into consideration such factors as adequacy of experimental design, statistical significance of the data, dose-response relations, duration of exposure, route of administration, metabolism (including species variations), host susceptibility, co-factors and other modifying factors, and the amount of material to which humans will be exposed." (18 refs.)

77-3605 **National Cancer Institute Workshop on Tumor Promotion and Cofactors in Carcinogenesis.** (Eng.) Weinstein, I. B. (Coll. Physicians and Surgeons, Columbia Univ., New York, NY 10032) Troll, W. *Cancer Res* 37(9): 3461-3463; 1977.

Biological models for studying the general properties of cancer-initiating and -promoting agents are discussed, with special reference to the tumorigenic activity in mouse skin experiments of some phorbol esters obtained from croton oil. (no refs.)

77-3606 **Pesticide Programs: Rebuttable Presumption Against Registration and Continued Registration of Pesticide Products Containing Diallate.** (Eng.) Conlon, J. M. (Office Pesticide Programs, Environmental Protection Agency, Washington, DC 20460) *Fed Regist* 42(104): 27669-27674; 1977.

Tests conducted on the herbicide diallate have indicated that there was an increased incidence of liver cell and pulmonary tumors in mice when the chemical was administered po. There was also a significant increase in the number of malignant tumors in rats receiving po diallate. Human exposure to this compound should be minimized. (28 refs.)

77-3607 **Carcinogens in the Workplace: Where to Start Cleaning Up.** (Eng.) Maugh, T. H. (No affiliation given) *Science* 197(4310): 1268-1269; 1977.

A recent study indicated that the manufacture of scientific and industrial instruments may be the most hazardous industry in the country, in terms of employee exposure to carcinogens. Even though the amount of carcinogenic materials used is small, the materials are used in hand fabrication, so that the total risk is high. Other highly hazardous industries and the carcinogens used in them are listed. (1 ref.)

77-3608 **Emergency Temporary Standard for Occupational Exposure to Benzene; Notice of Hearing.** (Eng.) Foster, J. (Office of Public Affairs, Occupational Safety and Health Admin., Third St. and Constitution Ave., N. W. Room N-3641, Washington, DC 20210) *Fed Regist* 42(85): 22516-22529; 1977.

The Occupational Safety and Health Administration of the Department of Labor proposed an emergency temporary standard governing employee exposure to benzene, to be effective from May 21, 1977. The standard is based on clinical and epidemiological data (summarized in this report) that conclusively establish that benzene exposure presents a leukemia hazard. Employee exposure to benzene is limited to 1 ppm in air, as an 8-hr time-weighted concentration, with a ceiling level of 5 ppm for any 15-min period during the 8-hr day. The emergency temporary standard further requires the measurement of employee exposure, engineering controls, protective equipment and clothing, employee training, medical surveillance, work practices, and record-keeping. The emergency standard is to be superseded by a permanent standard within 6 mo. (4 refs.)

77-3609 **The Importance of Occupational Cancer.** (Eng.) Boyland, E. (TUC Centenary Inst. Occupational Health, Lond Sch. Hygiene and Tropical Medicine, Keppel St., London WC1E 7HT, England) *Chem Eng* 569-570; 1977.

The incidence of occupational cancers among workers may act as warning signs to the general populace, because industrial causes of cancer may affect everyone. (no refs.)

77-3610 **Occupational Bladder Cancer (Letter to Editor).** (Eng.) Stellman, J. M. (Div. Occupational Health and Toxicology, American Health Foundation, New York, NY 10019) Hoffmann, D. *Lancet* 2(8037): 563-564; 1977.

It is possible that the high incidence of bladder cancer among men who work in the aluminum industry in the Province of Quebec is due to the presence of aromatic amines in the air. The products of coal tar pitch could be the source of these amines. (7 refs.)

77-3611 **Is the Operating Room Unhealthy (Letter to Editor)?** (Eng.) Cascorbi, H. F. (Dept. Anesthesiology, Case Western Reserve Univ. Sch. Medicine, Cleveland, OH) *JAMA* 238(9): 970; 1977.

The risk of malignant neoplasms in operating room personnel, particularly female anesthesiologists, may be due to the formation of nitrosamines due to the biotransformation of nitrous oxide. In addition, conformational changes of membranes as a result of the anesthesia itself may be responsible for faulty cell replication. (1 ref.)

77-3612 **Metals in Medicine and Surgery.** (Eng.) Mears, D. C. (Univ. Pittsburgh, Children's Hosp., Pittsburgh, PA) *Int Met Rev* 22(2): 119-155; 1977.

The risk of carcinogenesis after prolonged chronic exposure to various metals is reviewed. The incidence of malignant tumors resulting from metal implants in the bone could be greater because of the tendency of bone to form tumors or to be the seat of metastatic spread. However, carcinogenesis resulting from metal implants in humans is not a significant finding. (195 refs.)

77-3613 **Teratogenic Effects of Environmental Chemicals.** (Eng.) Wilson, J. G. (Children's Hosp. Res. Foundation, Cincinnati, OH 45229) *Fed Proc* 36(5): 1698-1703; 1977.

Although many drugs and chemicals are teratogenic in the laboratory, environmental concentrations are not generally sufficient to produce birth defects. Thalidomide, androgenic hormones, and folate antagonists are drugs known to be embryotoxic in humans. Methylmercury, however, is the only proved chemical, other than a drug, that causes developmental defects in man and has done so through its concentration in the food chain. (28 refs.)

77-3614 **Epidemiological Evidence on the Carcinogenic Risk of Air Pollution.** (Eng.) Higgins, I. T. *In: Environmental Pollution and Carcinogenic Risks.* (Lyon: International Agency for Research on Cancer): IARC Scientific Publications No. 13, INSERM Symposia Series Vol. 52, pp. 41-52; 1976.

The effects of air pollution on lung cancer occurrence are reviewed. The morbidity and mortality rates from lung cancer are known to be higher in urban as opposed to rural areas; this may be due to air pollution. For outdoor urban workers, the lung cancer risk appears to have increased. Surveys of differences in smoking habits and occupational exposure cannot explain such a wide margin between the frequency in urban and rural areas. It has been noticed that the death rate from lung cancer is lower among migrants, though their environmental exposures before migration are important. It is not certain if urban living enhances the lung cancer rate in nonsmokers. A decline in the lung cancer rate was noticed as pollution decreased in London. In attempts to relate lung cancer mortality rates to various pollution factors, eg, smoke, SO_2 hydrocarbons, and trace elements, the evidence was unsatisfactory. Air pollution may affect the lung cancer morbidity and mortality rates; however, its effect is small compared with the effect of smoking. (45 refs.)

77-3615 **Danger to Health from Air Pollution with Asbestos.** (Ger.) Dobbertin, S. (Berlin, W. Germany) *Staub Reinhalt Luft* 37(2): 65-67; 1977.

The biological effects of inhalation of asbestos fibers are reviewed. Data is presented on the extent of global air pollution by asbestos and the degree of contamination in humans from non-occupational exposure. Further investigations are necessary. (38 refs.)

77-3616 **Environmental Mutagenesis.** (Eng.) Fox, M. (Paterson Labs., Christie Hosp. and Holt Radium Inst., Manchester, England) *Nature* 268(5620): 488-489; 1977.

The deficiencies and advantages of currently available short-term tests for detecting environmental mutagens, which were discussed at the Second International Conference on Environmental Mutagenesis, are reviewed briefly. (12 refs.)

77-3617 **Detecting Mutagens--Correlation Between the Mutagenicity and Carcinogenicity of Chemicals.** (Eng.) Dybas, R. A. (Merck, Sharp & Dohme Res. Lab., Rahway, NJ 07065) Hite, M.; Flamm, W. G. *Annu Rep Med Chem* 12: 234-248; 1977.

Various mutagenicity tests for compounds, their validity and limitations are reviewed. The tests indicate that chemical-DNA interaction is necessary for some tumor inductions and that there is a definite link between mutagenic and carcinogenic events. (98 refs.)

77-3618 **Carcinogenic, Teratogenic, and Mutagenic Effects of Arsenic.** (Eng.) Bencko, V. (Dept. General and Environmental Hygiene, Medical Faculty Hygiene, Charles Univ., 10042 Prague, Czechoslovakia) *Environ Health Perspect* 19: 179-182; 1977.

A brief review of several studies dealing with the harmful effects of arsenic is presented. Discrepancies between previous inconclusive experimental results and clinical and epidemiological studies linking arsenic exposure to carcinoma indicate the need for new approaches. (50 refs.)

77-3619 **Cancer Susceptibility and Carcinogen Metabolism.** (Eng.) Gelboin, H. V. (NCI, Bethesda, MD 20014) *N Engl J Med* 297(7): 384-386; 1977.

Studies relating inducibility of aryl hydrocarbon hydroxylase (AHH), a catalyst in the detoxification of benzo(a)pyrene, to lung cancer are discussed. (24 refs.)

77-3620 **Drinking Water and Health: Recommendations of the National Academy of Sciences.** (Eng.) Blum, B. (Criteria and Standards Div., Office of Water Supply, Environmental Protection Agency, Washington, DC 20460) *Fed Regist* 42(132): 35764-35779; 1977.

Recommendations of the National Academy of Sciences concerning the contamination of water supplies with harmful substances are summarized. Four principles relevant to the assessment of risk from long-term exposure to carcinogenic substances at low doses are outlined: (1) effects in animals, properly qualified, are applicable to man; (2) methods to establish a threshold for long-term effects of toxic agents are not in existence; (3) the exposure of experimental animals to high doses of toxic agents is a necessary and valid method of discovering possible carcinogenic hazards in man; (4) materials should be assessed in terms of human risk, rather than as safe or unsafe. Risk estimates have been made for some known water supply contaminants for which data were available. Estimates of lifetime cancer risks (with a 95% upper confidence limit) are 5.1×10^{-7}, 2.6×10^{-4}, 4.4×10^{-4}, 1.2×10^{-6}, 3.1×10^{-6}, and 3.7×10^{-7} (expressed as risk/μg/liter) for vinyl chloride, dieldrin, kepone, DDT, polychlorinated biphenyls (with data for arochlor 1260), and carbon tetrachloride, respectively. The highest observed concentrations in drinking water of these substances are 10, 8, unknown, unknown, 3, and 366 μg/liter, respectively. The max observed levels of a large number of organic pesticides and other organic contaminants in drinking water are listed, together with recommended acceptable daily intake levels. (no refs.)

77-3621 **Coal Fires, Industrial Emissions and Motor Vehicles as Sources of Environmental Carcinogens.** (Eng.) Lawther, P. J.; Waller, R. E. *In: Environmental Pollution and Carcinogenic Risks.* (Lyon: International Agency for Research on Cancer): IARC Scientific Publications No. 13, INSERM Symposia Series Vol. 52, pp. 27-40; 1976.

The rural/urban difference in the concentrations of benzo(a)pyrene was for many years thought to be a notable factor in the occurrence of lung cancer; but now that industrial emissions and domestic smoke have been controlled considerably in Great Britain, the concentration of benzo(a)pyrene in the urban environment has been reduced by a factor of ten. In addition, traffic contribution to the benzo(a)pyrene level, although variable, is small in Great Britain. Correlations with a reduction in lung cancer are not yet possible, partly because recent cancers could have been induced by the former high levels and because the effect of cigarette smoking is now known to be an important etiological factor in lung cancer. Of other possible carcinogenic materials dispersed into the environment, asbestos has undergone the most investigation. The established association between asbestos and lung cancer and pleural mesothelioma is predominantly occupational; thus the general public is at very low risk. Similarly, many metals in trace amounts, eg, nickel, chromium, beryllium and vinyl choride monomer, are suspected of being occupational carcinogens. Careful monitoring of urban air is advisable when investigating possible etiologies of lung cancers. (37 refs.)

77-3622 **Air Pollution and Cancer.** (Ger.) Berndt, H. (Klinik fur innere Medizin, Bezirkskrankenhaus, Postfach 480, DDR-20 Neubrandenburg, E. Germany) *Arch Geschwulstforsch* 47(3): 259-271; 1977.

Air pollution is one of the environmental factors that either cause or, at the very least, exacerbate cancer development. At present, those air pollutants that are particularly dangerous have not been determined. However, there is a high risk of lung cancer in coal gas workers and a higher incidence of lung cancer in people living in urban and in industrialized areas compared to those living in rural areas. Young emigrating people have the lung cancer pattern of their country of origin, indicating that permanent damage is suffered in youth. Tobacco smoke inhalation is a more potent factor than air pollution. There is some evidence that air pollution causes cancer in the stomach and the prostate. (45 refs.)

77-3623 **Chemical Carcinogens.** (Fle.) van Wassenhove, F. (Laboratorium voor Organische Scheikunde, Fakulteit van de Landbouwwetenschappen, R.U.G., Ghent, Belgium) de Kimpek, N.; Schamp, N. *Ingenieursblad* 46(5): 121-130; 1977.

Some of the chemical carcinogens found in the environment are discussed and it is suggested that they account for 60% of all exogenous causes of malignancies. A brief description is given of inorganic compounds such as asbestos, aromatic amino compounds (β-naphthylamine), N-nitroso compounds, alkylating agents, aliphatic hydrazines, and aromatic hydrocarbons. A protocol is given for the determination of benzo(a)pyrene levels in grass. Naturally occurring carcinogens, such as those produced by molds (aflatoxin), bacteria (ethionine), and plants (cycasine), are described. The use of cell cultures as a quick method for evaluating the carcinogenic potential of new products is recommended. The need for caution in the manufacture and use of chemicals is stressed. (36 refs.)

77-3624 **Toxicology in Cancer Research. I. Carcinogenic Chemicals.** (Ger.) Schmahl, D. (Institut fur Toxikologie und Chemotherapie, Deutsches Krebsforschungszentrum, 6900 Heidelberg 1, Im Neuenheimer Feld 280, W. Germany) *Dtsch Med Wochenschr* 102(28): 1015-1018; 1977.

The role of chemicals as carcinogens is discussed, with emphasis on occupational exposure. Cancer may also be caused by environmental conditions in different parts of the world. The relation of smoking and air pollution to lung cancer is discussed, as is the effect of natural products such as the aflatoxins. The transplacental action of carcinogenic chemicals is established. (20 refs.)

77-3625 **Report on a Discussion Meeting on the Biology of Chemical Carcinogenesis.** (Eng.) Dulbecco, R. (Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England) *Proc R Soc Lond Biol* 196(1123): 117-130; 1977.

An interpretation is given of a discussion meeting on the biology of carcinogenesis held at the Royal Society of London on May 27, 28, 1976. The first topic was activation of chemical carcinogens in the animal body as related to site of action. In most situations, a cell undergoes neoplastic transformation as a result of activation of procarcinogens produced by the enzymes of the cell itself. In fact, concentration of the appropriate metabolizing enzymes in certain organs of certain species can be correlated to the sensitivity of these organs to cancer induction by different procarcinogens. Next, a review is given by Ames of his work on the development of bacterial tester strains from *Salmonella typhimurium* to detect mutagenesis caused by a variety of mechanisms. The mutagenicity of procarcinogens requires a liver extract to supply the metabolizing enzymes; many procarcinogens generate frame-shift mutagens, and the DNA targets with which each of them can effectively interact can be very different. Ames's results support the view that cancer results from somatic mutation. The assumption that mutations in somatic cells are the same as those observed in germ cells or in microorganisms is backed by several researchers. The role of karyotype changes in some types of mutations occurring in cultured cells was emphasized. Other subjects for discussion included transformation of cells in culture by chemical carcinogens, DNA repair, latent events in carcinogenesis, and alteration of gene expression in chemically induced cancers. (no refs.)

77-3626 **Chemical Carcinogenesis.** (Eng.) Heidelberger, C. (Los Angeles County-Univ. Southern California Cancer Center, 1721 N. Griffin Ave., Los Angeles, CA 90031) *Cancer* 40(1, Suppl): 430-433; 1977.

Many environmental carcinogens require activation by mixed-function oxidase to metabolites that form strong bonds with cellular macromolecules, initiating the carcinogenic process. DNA appears to be the main target for carcinogen interaction. The transformation of various cell lines is discussed. (49 refs.)

77-3627 **The *Ah* Locus and the Metabolism of Chemical Carcinogens and Other Foreign Compounds.** (Eng.) Thorgeirsson, S. S. (Developmental Pharmacology Branch, Natl. Inst. Child Health and Human Development, NIH, Bethesda, MD 20014) Nebert, D. W. *Adv Cancer Res* 25: 149-193; 1977.

An extensive review is presented of the properties of the *Ah* locus, the genetic locus (composed of 1 gene or a small number of genes) that controls the expression of cytochrome P_1-450, the enzyme responsible for aryl hydrocarbon hydroxylase (AHH) activity and that of several associated drug-metabolizing enzymes. Different alleles of the *Ah* locus have been recognized in different mouse strains. In vitro observations that are directly associated with the *Ah*b allele (as found in C57BL/6N mice) include: (1) the ability to metabolize 3-methylcholanthrene, 2-acetylaminofluorene, and 6-aminochrysene to mutagenic metabolites; (2) the occurrence of eight species of nucleoside-benzo(a)pyrene (BP) metabolite complexes after exposure of DNA to BP activated by microsomes from mice with the *Ah*b allele. AHH inducibility can be inherited in mice in either an autosomal dominant, additive (gene-dosage), or recessive mode, depending upon the strains of mice crossed. A list is presented of conditions (including cancer, drug toxicity, and birth defects) that are associated with the *Ah* locus in the mouse. (144 refs.)

77-3628 **Some Aspects of Teratogenesis and Mutagenesis in Mammalian Embryos.** (Eng.) Bass, R. (Institut fur Toxikologie und Embryonal-Pharmakologie, Freie Universitat Berlin, Garystrasse 9, 1000 Berlin 33, W. Germany) Bochert, G.; Merker, H. J.; Neubert, D. *J Toxicol Environ Health* 2(6): 1353-1374; 1977.

Model systems used to study the mechanism of action of toxic and mutagenic substances during prenatal development are reviewed. Growth of mouse limb buds in organ culture has permitted more extensive study of differentiation processes. The effect of a teratogen or mutagen depends on several pharmacokinetic parameters, which are discussed. Many mutagens and carcinogens belong to a class of substances whose effect is activated by a drug-oxidizing system in human fetal liver. The ability of fetal tissues to activate nitrosamines has been investigated by measuring the oxidation of dimethylnitrosamine (DMNA). Measurements using radioactive labeling of DNA indicate that alkylation in fetal tissues is about one order of magnitude lower than that found in adult tissues, whereas repair of alkylated DNA is considerably lower in fetal tissues. This could explain the sensitivity of fetal tissues to carcinogens applied transplacentally. Biochemical and morphological data indicate that the embryolethal action of chloramphenicol and thiamphenicol is due to their ability to inhibit mitochondrial protein synthesis. (21 refs.)

77-3629 **Sites in Nucleic Acids Reacting with Alkylating Agents of Differing Carcinogenicity or Mutagenicity.** (Eng.) Singer, B. (Dept. Molecular Biology, Univ. California, Berkeley, CA 94720) *J Toxicol Environ Health* 2(6): 1279-1295; 1975.

In vivo and in vitro alkylation of nucleic acids appears to occur at numerous sites, depending on the type of alkylating agent used. Recent work regarding the possible role of these sites in mutagenesis and carcinogenesis is reviewed. Poor carcinogens such as diethyl sulfate react with base nitrogens to form 7-ethylguanine. In studies with tobacco mosaic virus RNA treated with methylnitronitrosoguanidine, mutagenicity was correlated with the amount of 3-methylcytosine formed. Carcinogenic N-nitroso compounds show a great affinity for alkylating oxygens, and they react with internucleotide phosphodiesters as well as all ring oxygens. In RNA, the reaction of these compounds with the 2′-O of ribose could affect messenger RNA function by preventing normal processing. Neoplasms may develop in the brain of rats given methylnitrosourea or ethylnitrosourea (ENU) because O^6-alkylguanine remains in the DNA and mispairing occurs. Though less reactive than the corresponding methylating agents, ethylating agents show greater affinity toward oxygen. The very potent carcinogen ENU reacts primarily with oxygen regardless of whether the nucleic acid is single- or double-stranded. (44 refs.)

77-3630 **Nucleic Acid Alkylation, Mutation and Carcinogenesis: Is There a Relationship?** (Eng.) Singer, B. (Dept. Molecular Biology, Univ. California, Berkeley, CA 94720) *Trends Biochem Sci* 2(8): 180-183; 1977.

Current concepts of the oxygen affinity of alkylating agents indicate that this affinity may be related to carcinogenicity. The alkylation of nucleic acids and other cellular constituents may have an important influence on the neoplastic process. However, the initiating event is most likely genetic alteration of DNA as a result of mutation. (25 refs.)

77-3631 **N-Nitrosoamines (Letter to Editor).** (Eng.) Kothny, E. L. (Orinda, CA) *Chem Eng News* 55(19): 2; 1977.

Triethanolamine is an efficient collector of nitrogen dioxide and is suited for the collection and analysis of that gas in the environment. Nitroso derivatives that form during collection hydrolyze into nitrites, which can be reacted with azo-forming formulations such as the Saltzman reagent. It was therefore theorized that nitroso derivatives are easily formed during contact of di- and triethanolamines with contaminated air; ie, just by exposing the surface of cosmetic formulations to ambient air. (no refs.)

77-3632 **Formation of Nitrosamines in Food and in the Digestive System.** (Eng.) Wishnok, J. S. (Dept. Nutrition and Food Sciences, Massachusetts Inst. Technology, Cambridge, MA 02139) *J Chem Educ* 54(7): 440-442; 1977.

The mechanism by which nitrosamines initiate tumors is unknown, but it probably occurs through alkylation of DNA by an electrophilic metabolite of nitrosamine. Epidemiologic evidence links high local incidences of stomach cancer to high levels of dietary nitrate. These findings are discussed. (39 refs.)

77-3633 **Nitrate and Human Cancer.** (Eng.) Anonymous (No affiliation given) *Lancet* 2(8032): 281-282; 1977.

Populations consuming large amounts of nitrate have high mortality rates from gastric cancer. In Chile and Colombia, the prevalence of gastric achlorhydria may allow an increase in gastric flora, producing N-nitroso compounds and carcinogenesis. Urinary N-nitrosamine formation has also been linked with bladder cancer. (27 refs.)

77-3634 **New Study: Saccharin's a Carcinogen.** (Eng.) Anonymous (No affiliation given) *Med World News* 18(13): 36; 1977.

It is possible that the impurities in the laboratory chow fed the rats in the Canadian study on saccharin may have played a part in the production of bladder tumors. However, since saccharin is weakly carcinogenic in one species, it may also be carcinogenic in man, although the risk is not high. (no refs.)

77-3635 **Chloroquine.** (Eng.) IARC Working Group *In: IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Some Miscellaneous Pharmaceutical Substances.* International Agency for Research on Cancer (Lyon, France): Vol. 13, pp. 47-55; 1977.

Chemical and physical data; production, use, occurrence, and analysis; and available metabolic, mutagenic, toxicological, and carcinogenic data are given for chloroquine [CQ: N^4-(7-chloro-4-quinolinyl) -N′,N′-diethyl-1,4-pentadiamine], which is used to treat malaria, lupus erythematosus, and extraintestinal amebiasis. Only one animal carcinogenicity study has been performed, and the negative results obtained do not permit evaluation. In this study, groups of 21-day-old Osborne-Mendel rats were fed a diet containing 0-1,000 mg/

kg of CQ for up to 2 yr. Inhibition of growth was severe at the 800- and 1,000-mg/kg levels, but temporary at the 400-mg/kg level. All rats fed 800 or 1,000 mg/kg died within 35 wk. No tumors were seen in 86 treated rats or in 15 control rats examined microscopically. The oral LD50's of CQ phosphate are 620 mg/kg in mice, 970 mg/kg in rats, and 136 mg/kg in rabbits. CQ interacts noncovalently with DNA in vitro and inhibits mammalian DNA polymerase and DNA repair in both bacterial and mammalian cells. In man, high-dose long-term therapy with CQ can result in retinopathy and ototoxicity. The drug is well-absorbed from the gastrointestinal tract and is avidly retained in tissues. CQ and its metabolites (mainly de-ethyl-CQ) can be detected in urine for up to 5 yr after cessation of treatment. (42 refs.)

77-3636 **The Risks of Asbestos.** (Fre.) Boutin, C. (Service de pneumo-phtisiologie, Institut Paoli Calmettes, 232 Blvd. de Sainte-Marguerite, 13009 Marseille, France) *Rev Prat* 27(14): 867-869; 1977.

The difficulty of uncovering asbestos exposure, occupations in which exposure occurs, pathological manifestations of exposure (asbestosis, cancer, pleuroperitoneal mesothelioma), and practical measures for their treatment and prevention are discussed. (no refs.)

77-3637 **Studies on the Metabolism of Vinyl Chloride.** (Eng.) Antweiler, H. (Universitat Dusseldorf, Dusseldorf, W. Germany) *Environ Health Perspect* 17: 217-219; 1976.

Current ideas concerning the metabolism of vinyl chloride (VC) in mice and in humans are discussed. It is believed that VC is first metabolized by oxidases to chloroethylene oxide, a strong mutagen. Spontaneous conversion to chloroacetaldehyde (CA) follows; CA may be mutagenic and carcinogenic. Dehydrogenation of CA leads to chloroacetic acid (CAA), a substance of known toxicity but unknown mutagenicity. Conjugation of CAA with glutathione leads to the formation of the principal urinary metabolites of VC; namely S-carboxymethylcysteine and thiodiacetic acid. CAA may also be converted, via glycolic acid, to oxalic acid. (13 refs.)

77-3638 **Clinical Studies of Cancer Etiology.** (Eng.) Li, F. P. (35 Binney St., Boston, MA 02215) *Cancer* 40(1, Suppl): 445-447; 1977.

Careful clinical observation can lead to clues relating to cancer etiology. Among the more recent examples are the relationships between vinyl chloride and angiosarcoma of the liver, diethylstilbestrol and vaginal adenocarcinoma, and ataxia telangiectasia and the risk of lymphoreticular neoplasia. Interactions among physicians are encouraged. (22 refs.)

77-3639 **Liver Tumours and the Pill.** (Eng.) Anonymous (No affiliation given) *Br Med J* 2(6083): 345-346; 1977.

The exact association between liver tumors and ingestion of oral contraceptives is not clear, but women who take the pill for 5-7 yr apparently run a five times normal risk of development of these tumors. It is suggested that the estrogen components are important in the pathogenesis. (16 refs.)

77-3640 **Prevention of Endometrial Cancer (Letter to Editor).** (Eng.) Page, E. W. (Coll. Medicine and Dentistry New Jersey, Rutgers Medical Sch., Piscataway, NJ) *JAMA* 238(6): 481; 1977.

It is suggested that the use of oral contraceptives does not cause endometrial cancer, but rather prepares the endometrium for the development of cancer by preventing shedding. With the small-dose contraceptive now in use, it is not known if shedding will still be prevented or if cancer may develop from some other cause in the endometrium. (5 refs.)

77-3641 **Use of Estrogen Preparations after Menopause and the Risk of Endometrial Carcinoma.** (Dut.) de Waard, F. (No affiliation given) *Ned Tijdschr Geneeskd* 120(29): 1263-1264; 1976.

The increase in endometrial carcinoma during the last 20 yr and its possible causes are examined. Obesity and the concomitant continuous production of estrogen in adipose tissue are the main predisposing factors, because of their prevalence in the Western hemisphere. The noncyclic use of estrogen preparations by postmenopausal women increases the risk of endometrial cancer four- to sevenfold. This iatrogenic factor can be reduced by switching to cyclic therapy or to drugs with a lesser influence on the endometrium. (6 refs.)

77-3642 **Is the Aflatoxin Level in Peanut Butter Hazardous to Man?** (Eng.) Gilchrist, A. (AMA Dept. Foods and Nutrition, Chicago, IL) Fletcher, D. C. *JAMA* 238(6): 518; 1977.

Although aflatoxins appear to be one of the most potent experimental hepatocarcinogens known, there is no direct evidence that they cause cancer in man. With current technology, they cannot be eliminated from foods. The geographic distribution of liver cancer appears to bear no relationship to the distribution of aflatoxin in food materials in the US. (3 refs.)

77-3643 **Report of the Third International Symposium on Mycotoxins Held in Paris on 16-18 September 1976.** (Dut.) van Veldhuizen, C. J. (Food Inspection Dept., Rotterdam, Netherlands) *Voedingsmiddelentechnologie* 10(23): 8-9; 1977.

The legal limits for aflatoxins and similar compounds contained in grains and oil-bearing seeds in various countries, methods of sampling and analysis, new mycotoxins, prevention of contamination, detoxification and elimination procedures, and the need for inspection of human food and animal fodder are reported briefly. (no refs.)

77-3644 **Recommendations of the "Committee 17" on Environmental Mutagenesis: Implications to Radiation Safety.** (Eng.) Murthy, M. S. (Div. Radiological Protection, Bhabha Atomic Res. Centre, Trombay, Bombay 400 085, India) *Health Phys* 32(6): 567-569; 1977.

The use of radiation exposure limits as a guide for chemical exposure, as proposed by the Committee of 17, may be inadequate. Since chemical control can be achieved by eliminating the chemical, radiation should not be further restricted by a limit encompassing chemical exposure levels. (11 refs.)

77-3645 **Irradiation and Thyroid Carcinoma: Legacy and Controversy.** (Eng.) Frohman, L. A. (Div. Endocrinology and Metabolism, Michael Reese Medical Center, Chicago, IL 60616) *J Chronic Dis* 29(10): 609-612; 1977.

The association of thyroid carcinoma with prior x-irradiation of the head and neck is reviewed. A survey of 1,000 asymptomatic subjects (current mean age 33 yr) who had been irradiated primarily in the tonsils and nasopharyngeal region showed a 27% incidence of nodular thyroid disease. The results of surgical therapy have indicated that thyroid carcinoma is present in 33% of patients with nodular disease, giving a 9% projected incidence in the examined population. The carcinomas were papillary, follicular, or of mixed histology, and they were frequently multicentric, with extension through the thyroid capsule and metastases to adjacent lymph nodes. There was no evidence of distant metastases in the group. In nearly 80% of those with carcinoma, benign tumors were also present. (13 refs.)

77-3646 **Breast Carcinoma (Letter to Editor).** (Eng.) Nyirjesy, I. (Dept. Obstetrics and Gynecology, Georgetown Univ. Sch. Medicine, Washington, DC 20005) Burkons, D. M. *Obstet Gynecol* 50(2): 253-254; 1977.

The use of mammography to diagnose breast cancer is questioned because of the danger of inducing a cancer. A history, physical examination, and telethermography are suggested as diagnostic alternatives. In reply, it is pointed out that thermography is not always reliable and that mammography is being conducted with lower radiation exposure. (9 refs.)

77-3647 **The Viral Etiology of Cancer. A Realistic Approach.** (Eng.) Rapp, F. (Dept. Microbiology, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA 17033) Reed, C. L. *Cancer* 40(1, Suppl): 419-429; 1977.

There appear to be a number of predisposing factors (genetics, age, hormones, immune competence, stress) associated with viruses in the induction of cancer. The human cancers most strongly associated with a viral etiology include Burkitt's lymphoma, nasopharyngeal carcinoma, cervical carcinoma, acute myelogenous leukemia, and breast cancer. These factors and diseases are discussed. (53 refs.)

77-3648 **Virus and Cancer.** (Fre.) Monier, R. (Institut de Recherches Scientifiques sur le Cancer, Villejuif, France) *Rev Palais Decouverte* 5(49): 14-37; 1977.

The role of viruses in cancer is reviewed extensively. After a brief summary of viral research, the mechanisms of oncogenicity of DNA and RNA viruses are described along with the extensive research on simian virus 40. Host-virus specificity and phylogeny reveal the ancient association of viruses with mammalian hosts. The relationship of Epstein-Barr DNA virus to human cancers is discussed. Other human oncogenic viruses undoubtedly exist, but, according to the review, they have not been established definitely. The relative lack of success in the identification of human oncoviruses is probably due to technical inadequacies. (60 refs.)

77-3649 **The Relationship of Tumor Virology to an Understanding of Nonviral Cancers.** (Eng.) Temin, H. M. (McArdle Lab., Univ. Wisconsin, Madison, WI 53706) *Bioscience* 27(3): 170-176; 1977.

Current concepts regarding the mechanisms of carcinogenesis by viruses and chemicals are reviewed briefly. The following topics are discussed: viruses and cancer in animals; chemical carcinogens and human cancer; endogenous virus-related nucleotide sequences in cellular DNA; the replication of ribodeoxyviruses; variation of RNA tumor viruses; and the protovirus hypothesis. Nononcogenic RNA tumor viruses have evolved from the cell genome: the transforming genes of transforming RNA viruses have independently evolved from the cell genome. The replication of RNA tumor viruses involves the formation of a pool of free infectious viral DNA molecules. A high rate of genetic variation occurs in the replication of these viruses, probably during the formation of the pool of free viral DNA molecules. It is proposed that a similar system of information transfer with a high rate of genetic variation exists in normal cells and that genes involved in this transfer are the targets for most carcinogens. (43 refs.)

77-3650 **RNA Viruses, Genes, and Cancer.** (Eng.) Gallo, R. C. (Lab. Tumor Cell Biology, NCI, Bethesda, MD 20014) *Prog Cancer Res Ther* 3: 455-463; 1977.

Considerable evidence supports an etiologic role for RNA tumor viruses (oncornaviruses) in some naturally occurring mammalian neoplasms, especially leukemias and lymphomas. This report reviews the evidence and focuses on the myelogenous leukemias (ML). A schematic diagram is given of the proposed origin of RNA tumor viruses and how they may become oncogenic. The subhuman primate C-type RNA tumor viruses are singled out for discussion because they are the first C-type viruses to be obtained from animals closely related to humans, and highly related or identical viruses have been isolated from humans. Next, evidence for human C-type viruses or virus components is reviewed. Several reports show that fresh uncultured blood cells from some ML patients contain reverse transcriptase (RT) that in certain cases is related immunologically to the RT from the simian sarcoma virus-gibbon ape leukemia virus group. Other studies have detected high molecular wt RNA with nucleic acid sequences related to the RNA genome of some C-type viruses. This relationship is closest to the RNA of the primate C-type viruses. In recent studies, whole infectious C-type virus was isolated from the cells of ML patients. Immunological data taken at face value suggest that these viruses are widespread in the human population. Widespread infection may occur early in life, possibly in utero. By analogy with some animal models, it is proposed that viral information is causatively involved in ML but in a complex way that probably depends on other factors, such as host genetic traits, chance (infection of the right cell at the right time and integration into the right chromosomal site), and environmental inducing events. (44 refs.)

77-3651 **Endogenous C-Type Viruses in Normal and "Abnormal" Cell Development.** (Eng.) Levy, J. A. (Cancer Res. Inst., Univ. California Medical Center, San Francisco, CA 94143) *Cancer Res* 37(8, part 2): 2957-2968; 1977.

The potential role of endogenous C-type viruses in normal maturation (embryogenesis and differentiation) and aging processes (autoimmunity and cancer) is discussed. The host response and the extent of virus or viral antigen expression may determine the degree of normal maturation in the early stages of development as well as the type of condition occurring during the late stages of aging. C-type viruses have been identified by electron microscopy or isolated directly from a variety of vertebrates, which are listed. Although observed by electron microscopy in several human tissues, a confirmed human C-type virus has not yet been isolated. Viruses that have been implicated in cancers in animals and humans are tabulated. The latter include DNA and RNA viruses. The mouse model system has been useful for examining the role of endogenous viruses in nature, since the mouse develops diseases similar to those in humans and contains at least three types of endogenous C-type RNA viruses. Classified descriptively by their host range properties (ecotropic, xenotropic, and amphotropic), these viruses share some proteins and nucleic acid sequences in common, but they can be distinguished from one another by certain serological and molecular properties. Xenotropic viruses are present in early embryos, in cells undergoing normal differentiation, and in cancer cells. A nonimmunoglobulin factor that specifically neutralizes xenotropic viruses has been identified in normal mouse sera. Virus expression therefore appears to be regulated by intracellular as well as humoral factors. Viral proteins on the cell surface may be receptors for the transfer of information to the cell from its outside environment. (111 refs.)

77-3652 **Adenovirus Gene Expression--A Model for Mammalian Cells.** (Eng.) Philipson, L. (Dept. Microbiology, Biomedical Center, Uppsala Univ. S-751 23, Uppsala, Sweden) *FEBS Lett* 74(2): 167-173; 1977.

The following topics are discussed: maps of adenovirus (Ad) RNA sequences in the nucleus and cytoplasm of early infected cells, before the onset of DNA replication; maps of these sequences late after infection; the purification and in vitro translation of complement-specific Ad messenger RNA (mRNA); and the synthesis of low-molecular-wt RNA species in AD-infected cells. The complex organization of the AD2 genome and the extensive transcriptions of viral DNA, including sequences complementary to mRNA species, emphasize the role of posttranscriptional controls in the selection of specific mRNA species from a broader population of nuclear transcripts. (45 refs.)

77-3653 **The Topography and Transcription of the Adenovirus Genome.** (Eng.) Flint, J. (Dept. Biochemical Sciences, Princeton Univ., Princeton, NJ 08540) *Cell* 10: 153-166; 1977.

Methods by which adenovirus (ADV) gene products have been located on the viral genome are discussed. Consideration is given to mechanisms by which viral messenger RNA (mRNA) may be synthesized in ADV-infected and ADV-transformed cells. These mechanisms may mirror the usual mammalian modes of mRNA synthesis. The topography of the genome of C-type human ADV has been fairly well-defined. However, little is known about the structure of other ADV subgroups beyond a map of ADV12 mRNA sequences. Similar topographical features may be preserved in all human ADV. A great deal of evidence suggests that the primary transcription products of ADV2 DNA during the late phase of productive infection are extremely large molecules. Biogenesis of mRNA from these precursors would seem to require specific cleavages within them and modification of both the 3′ and 5′ ends of the sequences destined to function as mRNA. (126 refs.)

77-3654 **Species Identification and Genome Mapping of Cytoplasmic Adenovirus Type 2 RNAs Synthesized Late in Infection.** (Eng.) McGrogan, M. (Dept. Pathology, Div. Biology and Biomedical Sciences, Washington Univ. Sch. Medicine, St. Louis, MO 63110) Raskas, H. J. *J Virol* 23(2): 240-249; 1977.

Adenovirus type 2 (Ad2) cytoplasmic RNA's synthesized late in the productive infection of KB cells were resolved by electrophoresis on formamide gels. Regions of the Ad2 genome specifying RNA's of distinct size were determined by hybridization to specific DNA fragments generated by cleavage with endo R.*Eco*RI and endo R.*Sma*I. From these studies, 13 distinct viral RNA species were identified. A 26S to 28S size class and a 21S to 23S class were each found to consist of four distinct RNA species. Three RNA species were identified in a 16S to 18S class, and a fourth class, 11S to 13S, was resolved into two components. The *Sma*I-D region (0.38 to 0.51 on the unit genome) and the *Eco*RI-F, D region (0.70 to 0.83) of the genome were found to code for multiple transcripts. Three RNA's (28S, 22S, and 18S) are specified by *Sma*I-D, and four components, 28S, 22S, 18S, and 16S, are encoded by *Eco*RI-F,D. The RNA represented by each set of multiple transcripts exceeds the coding capacity of the respective region, and the species within each set of RNA's appear to contain common sequences. The relationship between the cytoplasmic RNA species synthesized at late times and early cytoplasmic RNA's was determined by hybridization-inhibition experiments. The multiple transcripts encoded by the *Eco*RI-D fragment contained sequences that are present in early cytoplasmic RNA. These studies enable preparation of a map that accounts for transcription of approx 67% of the *r* strand of the Ad2 genome. (50 refs.)

77-3655 **Herpes Simplex--Oncogenesis, Epidemiology, Diagnosis, and Therapy: An Introduction.** (Ger.) Nasemann, T. (Zentrums fur Dermatologie und Venerologie der J. W. Goethe-Universitat, Theodor-Stern-Kai 7, 6000 Frankfurt am Main, W. Germany) *Z Hautk* 52(7): 413-415; 1977.

Two main types of herpes simplex virus are known: type 1 occurs predominantly on the face and mucous membranes of the mouth; type 2, on the genital and gluteal areas. Type 2 is comprised of subtypes α and β, with the latter being of possible oncological importance. Experiments with inactivated virus and new experiments with attenuated live virus are compared. (no refs.)

77-3656 **Herpes Simplex Virus Type 2.** (Eng.) Anonymous (No affiliation given) *Arch Intern Med* 137(5): 562; 1977.

At least 19 strains of herpes virus type 1 have been reported, and perhaps as many strains of type 2. Herpes virus type 2, in combination with predisposing factors, may cause cervical cancer in women whose sex partners transmit such a factor. (no refs.)

77-3657 **Anatomy of Herpes Simplex Virus DNA. VIII. Properties of the Replicating DNA.** (Eng.) Jacob, R. J. (Marjorie B. Kovler Viral Oncology Labs., Univ. Chicago, Chicago, IL 60637) Roizman, B. *J Virol* 23(2): 394-411; 1977.

The properties of herpes simplex virus 1 DNA replicating in HEp-2 and human embryonic lung cells were determined. Only a small fraction of input viral DNA entered the replicative pool. The bulk of the input viral DNA cosedimented with marker viral DNA and did not appear to be degraded or dissociated into L and S components. Nascent DNA sedimented faster and banded at a higher density than mature viral DNA extracted from virions. Pulse-chase experiments indicated that nascent DNA acquires the sedimentation rate and buoyant density of viral DNA within 30 to 40 min after its synthesis. Electron microscopic studies indicated that the DNA extracted from cells replicating viral DNA and banding at the density of viral DNA contained: (1) linear, full-sized molecules with internal gaps and single-stranded regions at termini; (2) molecules with lariats, consisting of a linear segment up to two times the size of mature DNA and a ring ranging from 0.5×10^6 to 100×10^6 in molecular wt, showing continuous and discontinuous forks; (3) circular, double-stranded molecules, both full-sized and multiples of 18×10^6 in molecular wt, but without forks or loops; (4) molecules showing "eye" and "D" loops at or near one end of the DNA; (5) large, tangled masses of DNA, similar to those observed for T4 and pseudorabies virus replicating DNA's, containing loops and continuous and discontinuous forks. The electron micrographs are consistent with the hypothesis that the single-stranded ends on the DNA anneal to form a hairpin, that DNA synthesis is initiated at or near that end and proceeds bidirectionally to form a lariat, and that resulting progeny derived by semiconservative replication are head-to-head and tail-to-tail dimers. (27 refs.)

77-3658 **Molecular Biology of Papovaviruses.** (Eng.) Fareed, G. C. (Molecular Biology Inst., Univ. California, Los Angeles, CA 90024) Davoli, D. *Annu Rev Biochem* 46: 471-522; 1977.

The proteins, genomes, replication, transcription properties, mutants, and sequencing of polyoma virus and simian virus 40 are reviewed. The human papovaviruses DAR, JC, and BK are also considered. (423 refs.)

77-3659 **An Analysis of the Role of tRNA Species as Primers for the Transcription into DNA of RNA Tumor Virus Genomes.** (Eng.) Taylor, J. M. (Inst. Cancer Res., Fox Chase Cancer Center, 7701 Burholme Ave., Philadelphia, PA 19111) *Biochim Biophys Acta* 473(1): 57-71; 1977.

Findings regarding the early events in the in vitro transcription of viral RNA into DNA are reviewed. Discussion is made of the RNA tumor virus genome; identification of a transfer RNA (tRNA) primer for in vitro transcription into DNA; interaction between the tRNA primer and viral 35S RNA; initiation of transcription on the tRNA primer; RNA primer involvement in the synthesis of uniform DNA transcripts; large DNA transcripts initiated on a tRNA primer from a common origin on the genome; the in vivo role of tRNA primers; and the mechanism by which genome-sized transcripts are generated. (73 refs.)

77-3660 **The Reverse Transcriptase.** (Eng.) Verma, I. M. (Tumor Virology Lab., Salk Inst., Post Office Box 1809, San Diego, CA 92112) *Biochim Biophys Acta* 473(1): 1-38; 1977.

A comprehensive review is presented of the properties of reverse transcriptase (RT). The following topics are covered: the life cycle of RNA tumor viruses; purification of RT enzymatic activities associated with purified RT; the structure of RT in avian and murine systems, reticuloendotheliosis virus, and hamster leukemia virus; immunological properties of RT; RT inhibitors; coding for RT by the viral genome; the temperature-sensitive replication-defective mutant of Rous sarcoma virus, LA762; mouse sarcoma viruses; intracellular RT; diagnostic features of RT; reverse transcription with viral RNA or natural RNA's as template, and transcription of RNAs lacking poly(A); future RT research trends. (204 refs.)

77-3661 **Reading the Tumour Virus Genome.** (Eng.) Mahy, B. W. (Dept. Pathology, Univ. Cambridge, Cambridge, England) *Nature* 268(5619): 398-399; 1977.

The results of several studies indicate that the only open cistron that is available for translation from the 35S genome of RNA oncornaviruses is the *gag* gene, located nearest to the 5′ end. Sites for the other gene products appear to be blocked. (22 refs.)

77-3662 **Immune Surveillance Against Virus-induced Tumors and Nonrejectability of Spontaneous Tumors: Contrasting Consequences of Host Versus Tumor Evolution.** (Eng.) Klein, G. (Dept. Tumor Biology, Karolinska Inst., S 104 01, Stockholm 60, Sweden) Klein, E. *Proc Natl Acad Sci USA* 74(5): 2121-2125; 1977.

The possible effects of natural selection in modifying host immune responsiveness to neoplastic changes in the host cell are discussed. Natural selection for host recognition of commonly occurring, virally induced changes in neoplastic cell membranes must occur in order for protection to be provided against the oncogenic effects of ubiquitous tumor viruses in hosts of all ages. On the other hand, most spontaneous tumors do not precipitate strong immune reactions, as do most virally induced tumors. Here, natural selection cannot play a major role in making host immune resistance effective to the subtle neoplastic changes involved, because most naturally occurring tumors arise after the host has passed the peak of its reproductive period. The unresponsiveness of host immune systems to spontaneous tumors may be overcome by (1) chemical modification of the tumor cell membranes, particularly by the coupling of haptens or other strong antigens, (2) virally induced "xenogenization", or (3) biological coupling of the tumor cell membranes to strongly alloantigenic or xenoantigenic partners by somatic cell hybridization. (49 refs.)

77-3663 **Antigens, Immunoglobulins, and Immunity During the Course of Breast Cancer.** (Eng.) Order, S. E. (Johns Hopkins Radiation Oncology Center, Baltimore, MD 21205) *Progr Clin Biol Res* 12: 119-130; 1977.

A review is given of the pretreatment immune status of breast cancer patients; antigenic characteristics of the primary tumor; lymphocytes and radiation therapy, hormones, and immunity; immunoglobulins; and clinical intervention with isotopic immunoglobulins. (64 refs.)

77-3664 **Blood Group Mythology: Present Status.** (Eng.) Wiener, A. S. (Serological Lab., Office of Chief

Medical Examiner of New York City, New York, NY) *Acta Genet Med Gemellol (Roma)* 26(1): 3-15; 1977.

The false associations between blood groups and cancers of various locations are discussed. (23 refs.)

77-3665 **Morphogenesis and Cancer.** (Eng.) Burnet, F. M. (Dept. Microbiology, Univ. Melbourne, Parkville, Victoria 3052, Australia) *Med J Aust* 1(1/2): 5-9; 1977.

The role of a somatic mutation in cellular DNA as a cause of cancer is briefly reviewed. Various topics include cancer as a genetic error, developmental processes and cancer, and environmental agents and cancer. The role of somatic mutations in differentiation is also discussed. (10 refs.)

77-3666 **Chromosomes and Cancer.** (Eng.) Anonymous (No affiliation given) *Lancet* 2(8031): 227-228; 1977.

The associations between various chromosomal abnormalities and cancer, especially the Philadelphia chromosome and chronic myeloid leukemia, are reviewed. The various translocations and the association between genetic disorders and malignant disease are discussed. (57 refs.)

77-3667 **Relationship Between Differentiation and Carcinogenesis.** (Eng.) Pierce, G. B. (Dept. Pathology, Univ. Colorado Medical Center, 4200 E. Ninth Ave., Denver, CO 80262) *J Toxicol Environ Health* 2(6): 1335-1342; 1977.

The hypothesis that cancer is a postembryonic differentiation that is a caricature of the tissue of origin is discussed. Several experiments with embryonal carcinoma have demonstrated that highly malignant stem cells can give rise to normal progeny. The undifferentiated appearance of most carcinomas results from a preponderance of undifferentiated stem cells in relationship to differentiated cells. In studies of adenocarcinomas of the breast and colon, normal stem cells appeared to be no more differentiated than stem cells of corresponding cancers. The difference in biological behavior of benign and malignant cells may depend on a critical number of cells necessary for differentiation to occur. Perhaps highly electrophilic molecules react with cytoplasmic components to activate large pieces of heterochromatin, carrying the repressed genetic information essential for development and neoplasia. The concept of changes in the genome itself or somatic mutation as a cause of cancer warrants further study. (19 refs.)

77-3668 **Cell Locomotion and Tumor Penetration: Report on a Workshop of the EORTC Cell Surface Project Group (Zurich, 8-10 April 1976).** (Eng.) Strauli, P. (Div. Cancer Res., Inst. Pathology, Univ. Zurich, Birchstrasse 95, 8050 Zurich, Switzerland) Weiss, L. *Eur J Cancer* 13(1): 1-12; 1977.

The role of active locomotory movement in tumor penetration is evaluated, and aspects of cell locomotion and tumor penetration from morphological, biophysical, and biochemical viewpoints are considered. Topics of discussion include evidence for cell locomotion in tumor penetration, the concept of tumor cell mobilization, proliferation and locomotion of tumor cells, the relationship between the locomotive tumor cell and its environment, and the locomotive apparatus of the nonmuscular mammalian cell. The locomotion of tumor cells most likely depends on the operation of the actin/myosin system, but the relationship of data concerning the presence and nature of contractile proteins in these cells to cell movement and cell infiltration is yet unclear. (77 refs.)

77-3669 **Spread and Behavior of Cancer and Staging.** (Eng.) Davies, J. N. (Div. Oncology, Albany Medical Coll. Union Univ., Albany, NY) *In: Clinical Oncology.* Horton, J.; Hill, G. J., eds. (Philadelphia: W. B. Saunders Co.) pp. 34-49; 1977.

The major clinical problems of cancer are caused by the propensity of the new growths to spread locally, regionally, and distantly. Increase in size is a consequence of cell division. One problem of carcinogenesis is that cells that divide to produce the cancer may never have been stimulated by any directly acting carcinogen. They may be the progeny of several generations of cell division after exposure to a chemical carcinogen many years previously. The rate of cell division determines the growth of a cancer. Local spread is infiltrative, either slowly erosive or involving hemorrhagic necrosis, ulceration, and fibrous replacement of the invaded tissue. Local spread is a prerequisite to metastasis. Disseminative metastatic spread occurs by the planes of tissue cleavage, lymph channels, blood vessels, celomic cavities, cerebrospinal pathways, and epithelial cavities. Metastasis via the lymphatics and blood stream is singled out for discussion. There is a high degree of histologic, cytologic, and functional agreement between the primary cancer and metastases. This review concludes with a survey of the classification of cancer. One classification is by histiogenesis and biologic behavior into five major groups: tumors of (1) epithelial, (2) nonhematopoietic mesenchymal, (3) hematopoietic and lymphoid and (4) neural tissues and (5) miscellaneous tumors. Another system, the TNM classification (T, primary tumor; N, lymph node involvement; M, distant metastasis), and an illustration of its use in the staging of breast cancer are given in tabulated form. (19 refs.)

77-3670 **Solitary Rectal Polyp--A Disease with Cancer Risk?** (Ger.) Junemann, A. (Chirurgische Universitatsklinik A, Moorenstrasse 5, D-4000 Dusseldorf, W. Germany) Muller, E. *Med Klin* 72(8): 286-293; 1977.

Review of the diagnosis and treatment of 100 patients with solitary rectal polyps showed that 18%-20% had similar polyps and carcinomas in other sites in the colon. Excision must be performed because of the problem of malignant transformation and the high tendency to polyp recurrence. (109 refs.)

77-3671 **The Parathyroid Glands.** (Eng.) Wang, C. (Massachusetts General Hosp., Boston, MA) Cope, O. *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 256-264; 1976.

Functional cases of parathyroid gland carcinoma associated with evidence of hyperparathyroidism (HPT) are reviewed. Of 584 primary HPT patients, 19 cases of parathyroid carcinoma were diagnosed. As the metabolic disturbance progressed, multiple complications occur. Renal involvements, skeletal lesions or spontaneous fractures were common; peptic ulcer and pancreatitis often appeared in the terminal stage. The location of the primary tumor varied: 8 tumors were found in the lower neck, 3 in the superior mediastinum, and 6 in the upper neck. The size of the primary tumor also varied. Additional pathologic features are described along with the biologic nature of the disease, its incidence, criteria for diagnosis,effective treatment and resulting prognosis. (38 refs.)

77-3672 **Progress Report. Cancer of the Pancreas.** (Eng.) Morgan, R. G. (Dept. Physiology, Univ. W. Australia, Nedlands, W. Australia) Wormsley, K. G. *Gut* 18(7): 580-596; 1977.

Various etiological factors influencing the development of pancreatic cancer include cigarette smoking, diet, diabetes mellitus, pancreatitis, and various chemical carcinogens (result of animal studies). The incidence, diagnosis, and prognosis of this cancer are also reviewed. (140 refs.)

77-3673 **Spontaneous Tumors of the Uterus and Ovaries in Animals.** (Eng.) Cotchin, E. (Dept. Pathology, Royal Veterinary Coll., Univ. London, Camden Town, London NW1 OTU, England) *In: Animal Tumors of the Female Reproductive Tract: Spontaneous and Experimental.* Cotchin, E.; Marchant, J. (New York: Springer-Verlag) pp. 26-65; 1977.

The incidence of spontaneous tumors of the uterus and ovaries in wild, domestic, and laboratory animals is reviewed. Compared to humans, carcinoma of the cervix is rare in animals, suggesting that the cause of this cancer in women is probably specific for the human tumor. (219 refs.)

77-3674 **Animal Models for Tumors of the Ovary and Uterus.** (Eng.) Marchant, J. (Regional Cancer Registry, Queen Elizabeth Medical Centre, Birmingham B15 2TH, England) *In: Animal Tumors of the Female Reproductive Tract: Spontaneous and Experimental.* Cotchin, E.; Marchant, J. (New York: Springer-Verlag) pp. 1-25; 1977.

Various animal models that are used for tumors of the ovary, uterine fundus, placenta, uterine cervix, vagina and vulva are presented. The efficacy of laboratory animals as hosts for human tumor transplants (hamster cheek pouch and immune-suppressed mouse) is discussed briefly. (201 refs.)

77-3675 **Oestrogen-like Activity and Cervical Atypias (Letter to Editor).** (Eng.) Rubio, C. A. (Inst. Pathology, Karolinska Sjukhuset, 104 01 Stockholm 60, Sweden) *Lancet* 2(8030): 188-189; 1977.

Studies of patients with cervical atypias and malignant or benign cervical disease indicated that there was increased maturation of normal squamous cells in patients with atypias. Whether the maturation occurs before or after the atypia is unknown. (7 refs.)

77-3676 **Estrogen and Progesterone: Their Relationship in Hormone-dependent Breast Cancer.** (Eng.) Horwitz, K. B. (Univ. Texas Health Science Center, San Antonio, TX 78284) McGuire, W. L. *Prog Cancer Res Ther* 4: 103-124; 1977.

The role of estrogen and progesterone receptors in animal and human breast cancers is reviewed. Although 75% of human mammary tumors appear to be estrogen receptor-positive, primary tumors are more likely to be so than metastatic ones. The significance of this finding is discussed. (109 refs.)

77-3677 **The Breast.** (Eng.) Moore, F. D. (Peter Bent Brigham Hosp., Boston, MA) *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 265-304; 1976.

During the past 15 yr, breast cancer has emerged in the US as the commonest malignant tumor of women and the commonest cause of death of white women aged 40-65 yr. One of every two patients initially seen with the disease will be dead from this cause within 5 yr. Approx 60,000 new cases are discovered each year, an incidence of 55/100,000 women. The age-adjusted mortality rate is 25/100,000. The etiologic background has a three-sided aspect: genetic factors, endocrine setting, and carcinogenic factors such as external ionizing radiation or possible virus involvement. Some breast cancers are very slow-growing and noninvasive, but others are highly malignant, causing death within months of discovery. These different types have given rise to the concept of biological predeterminism, and if the tumor doubling time could be known, the physician would know where the patient was situated in the invasive spectrum of the disease. Early diagnosis by breast self-examination, mass screening, and radiological examinations ranging from mammography to xeroradiography are discussed. Among the other topics covered in this review are clinical modes of presentation, family history, aspects of the physical examination, the value and techniques of biopsy, clinical differential diagnosis alternatives among malignant tumors (well-differentiated and slowly growing, typically malignant infiltrating, or the highly malignant undifferentiated tumor with many mitoses and multinucleated giant cells) and alternatives to malignancy, primary treatment (plus follow-up, radiotherapy, and chemotherapy), treatment of advanced local disease without distant metastasis, and treatment of recurrent or metastatic disease. (82 refs.)

77-3678 **Predominance of Left-sided Breast Tumours (Letter to Editor).** (Eng.) McManus, I. C. (Psychological Lab., Univ. Cambridge, Cambridge CB2 3EB, England) *Lancet* 2(8032): 297-298; 1977.

A significant predominance of left-sided tumors has been found in North American and European breast cancer patients. Genetic studies have indicated that a relative is more likely to be affected in the same breast as the propositus only if the propositus had a left-sided tumor. Cancers of the left breast also tend to be adenocarcinomas. It is suggested that laterality be included in tumor classification. (10 refs.)

77-3679 **Tissue Culture and Transplantation of Breast Cancer.** (Eng.) Ozzello, L. (Dept. Pathology, Univ. Lausanne, 1011 Lausanne, Switzerland) *Progr Clin Biol Res* 12: 55-70; 1977.

The use of various cell cultures, organ cultures, and heterotransplantation techniques for the study of human mammary cancer is reviewed. These techniques provide useful knowledge without violating any ethical research principles. Their applications are discussed. (63 refs.)

77-3680 **Determination of Population Groups with a High Risk of Breast Cancer.** (Ger.) van der Linde, F. (Sanitatsdepartement des Kantons St. Gallen, Moosbruggstrasse 11, CH-9001 St. Gallen, Switzerland) *Schweiz Med Wochenschr* 107(28): 962-968; 1977.

The following risk factors for breast cancer are discussed: sex, age, race, religion, social status, marital status, pregnancy, ovariectomy, menopause, menarche, hormonal functions, genetic effects, and predisposing diseases. The differentiation between high and low risk is not sufficient to exclude any group from prophylactic measures. (63 refs.)

77-3681 **'What Are My Chances of Getting Breast Cancer?'** (Eng.) Bernstein, T. C. (Div. Hematology-Oncology, Scripps Clinic and Res. Foundation, 10666 N. Torrey Pines Road, La Jolla, CA 92037) *JAMA* 238(4): 345-346; 1977.

Although the chances of a woman developing breast cancer are 1 in 15, there are many factors that influence this chance. These factors include: age at menarche, menopause, and first pregnancy; multiparity; diet; hypothyroidism; benign breast diseases; environment and heredity. (no refs.)

77-3682 **Breast Cancer--Patients at Risk.** (Eng.) Leis, H. P. (Dept. Surgery, NY Medical Coll., NY) *Cancer Detect Prevent* 1(2): 311-330; 1976.

Development of breast cancer seems to be due to the interplay of many single risk factors. The major ones are sex, with 99% of all cases occurring in women; age, with 75% occurring in women > 40; familial history (particularly for the premenopausal bilateral form of the disease); parity, with emphasis on age at first pregnancy; previous cancer in one breast; and the precancerous mastopathy type of fibrocystic disease. The prominent risk factors include adverse hormonal milieu, lack of immunological competence, excessive radiation exposure to the breast, and carcinogen exposure, including viruses and other agents such as reserpine. Patients with an adverse hormonal milieu are those with prolonged menstrual activity, lowered estriol fraction, or subnormal levels of etiocholanolone and/or androsterone, nulliparous or late parous women who received exogenous estrogens, hypothyroid patients, and patients who are obese, diabetic, and hypertensive. A lack of immunological competence can be found in older patients with thymic atrophy, patients with decreased thymus-dependent T lymphocytes, those with chronic psychological stress, those who have received radiotherapy to the breast or chemotherapy, and those who have received immunosuppressant drugs. (66 refs.)

77-3683 **Radiation and Breast Cancer (2 Letters to Editor).** (Eng.) Kalisher, L. (Massachusetts General Hosp., Harvard Medical Sch., Boston, MA) Greenes, R. A.; Simon, N. *JAMA* 238(7): 579-580; 1977.

A previously observed association between radiation treatment for acne and subsequent breast cancer in 16 young women is criticized on the grounds that data were insufficient for asserting a causal link. Mammography should be avoided in young women; however, the effects of low-dose radiation in the development of breast cancer are controversial. While more detailed statistical studies are needed, clinical observations of possible radiation effects may provide valuable preliminary evidence that radiation may indeed induce breast cancer. (2 refs.)

77-3684 **Thyroid Supplementation for Hypothyroidism. An Iatrogenic Cause of Breast Cancer?** (Eng.) Mustacchi, P. (Dept. International Health, Univ. California, San Francisco, CA 94143) Greenspan, F. *JAMA* 237(14): 1446-1447; 1977.

Data from an epidemiological study failed to find an association between breast cancer and thyroid supplementation. Only a uniform deficit of observed cancer incidence for all groups $<$ 46 yr and an excess among women $\geq$ 46 yr were found. (3 refs.)

77-3685 **The Vulva and the Vagina.** (Eng.) Way, S. (Dept. Gynecological Oncology, Univ. Newcastle upon Tyne, Newcastle upon Tyne, England) *In: Management of the Patient with Cancer. 2nd ed* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.): pp. 674-681; 1976.

Malignant tumors of the vulva and vagina, which are relatively rare, are discussed. Cancer of the vulva occurs in an older age group than other gynecological tumors. Its etiology is unknown, but it is frequently preceded by a variety of skin diseases. Malignant lesions of the vulva are predominantly squamous in type, followed by malignant melanoma. Vulval metastases to the lymph nodes, liver, lung, brain, and gastric mucosa are not uncommon. Forty-two percent of vulval cancers show lymphatic spread when first seen. Primary malignant disease of the vagina is very rare; secondary malignant disease is much more commonly encountered because of the spread of carcinoma of the cervix. Most primary vaginal carcinomas are squamous. Primary adenocarcinoma is sometimes seen and, in young girls, has been connected with the ingestion of synthetic estrogens by their mothers during pregnancy. Sarcoma of the vagina is even rarer, and malignant melanoma as a primary tumor is rarest of all. Symptoms of vaginal carcinoma are irregular vaginal bleeding and vaginal discharge. The only sign is a lump, exophytic or ulcerative, somewhere in the vagina. In addition to secondary vaginal cancer from the spread of cervical cancer, other secondary tumors are seen in the upper and lower third of the vagina. Those in the upper third are almost always adenocarcinomas, the primary being in the corpus uteri. The most common origins for the primary lesions in cases of secondary vaginal cancer in the lower third are carcinoma of the corpus uteri, carcinoma of the large bowel, renal cell carcinoma, and chorioepithelioma. (21 refs.)

77-3686 **Oestrogen-like Activity and Cervical Atypias (Letter to Editor).** (Eng.) Singer, A. (Dept. Obstetrics and Gynecology, Univ. Sheffield, Jessop Hosp. Women, Sheffield S3 7RE, England) Jordan, J. A. *Lancet* 2(8033): 359; 1977.

The validity of evidence that oral estrogens affect the cervicovaginal epithelium is questioned. It is proposed that development of thicker, more differentiated epithelium with irregular papillae protruding into the stroma is related to sexual behavior, which may cause trauma to the cervix or transmit some mutagen. (8 refs.)

77-3687 **Menopausal Estrogens and Genital Cancers (Letter to Editor).** (Eng.) O'Connor, J. A. (477 N. Harbor Drive, Indian Rocks Beach, FL 33535) *Am J Obstet Gynecol* 128(8): 925-926; 1977.

Two observations suggest that two types of female reproductive cancers exist. First, castration of premenopausal women with metastatic breast cancer often produces remission and, second, some breast cancers contain proteins that bind estradiol and other natural estrogens necessary for development of these tumors. Therefore, one type is dependent on the presence of estrogens and the other is not. (3 refs.)

77-3688 **Estrogen and Endometrial Carcinoma.** (Eng.) Knab, D. R. (Dept. Obstetrics and Gynecology, Uniformed Services Univ. Health Sciences, Bethesda, MD 20014) *Obstet Gynecol Surv* 32(5): 267-281; 1977.

The role of estrogens in endometrial carcinoma (EC) is reviewed. Discussion is made of the biological effects of estrogen from gonadal or extragonadal sources, the hypothalamic control of endogenous estrogen, the effects of exogenous estrogen in animals and in humans, and estrogen receptor sites. The following points are considered pertinent: estrogen-secreting tumors of the ovary are associated with EC; EC is frequently associated with polycystic ovarian disease; EC patients have an increased peripheral conversion of δ4-androstenedione to estrone (ie, 0.1% vs 0.027%); EC is associated with hypothalamic hyperactivity; patient suscepti-

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bility is important to EC development; long-term exogenous estrogen appears to cause malignant changes in the endometrium. (187 refs.)

77-3689 **Oestrogen Therapy and Endometrial Cancer (Letter to Editor).** (Eng.) Utian, W. H. (Dept. Reproductive Biology, Case Western Reserve Univ. Sch. Medicine, Cleveland, OH) *Br Med J* 2(6086): 577-578; 1977.

The use of estrogens for short-term relief of menopausal symptoms is defended. It is suggested that their use does not present an increased risk of endometrial cancer, providing that frequent reevaluations are taken and proper selection of drug, dosage, and therapeutic regimen is considered in patients with no contraindications. (9 refs.)

77-3690 **Cancer Induction by Exogenous Hormones. Possible Androgen-induced Cancer.** (Eng.) Antunes, C. M. (Dept. Epidemiology, Johns Hopkins Univ. Sch. Hygiene and Public Health, Baltimore, MD 21205) Stolley, P. D. *Cancer [Suppl]* 39(4): 1896-1898; 1977.

Ingestion of male hormones as anabolic steroids and oral contraceptives is associated with a large number of liver tumors. Because of the widespread use of these compounds, studies are necessary to investigate their etiological relationship to cancer. (23 refs.)

77-3691 **Malignant Testicular Tumors in Children (Letter to Editor).** (Eng.) Nelson, R. P. (Dept. Urology, Medical Univ. South Carolina, 80 Barre St., Charleston, SC 29401) *Urology* 10(3): 290; 1977.

Although prepubertal embryonal cell carcinoma is less likely to metastasize than its adult counterpart, metastases that do occur are usually more difficult to control. These childhood metastases are more likely to result from hematogenous rather than lymphatic spread. (1 ref.)

77-3692 **Immunological Deficiency and the Risk of Cancer.** (Eng.) Anonymous (No affiliation given) *Br Med J* 2(6088): 654; 1977.

Children with primary immune deficiencies have a hundredfold greater chance of developing cancer than normal children. The increased risk appears especially high for the lymphoreticular tumors, especially B and T cell types. Patients with iatrogenic immunodepression also have an increased risk of cancer, mostly for epithelial tumors. The mechanism behind these increased risks is unknown. (9 refs.)

77-3693 **Clinical Patterns of Familial Cancer.** (Eng.) Fraumeni, J. F. (Environmental Epidemiology Branch, NCI, Bethesda, MD 20014) *Prog Cancer Res Ther* 3: 223-233; 1977.

Cancer-prone families provide research opportunities that may clarify the role of genetic mechanisms in carcinogenesis. A small but increasing percentage of cancers (monogenic syndromes) are being recognized that exhibit Mendelian patterns of inheritance. Hereditary neoplasms are autosomal dominant traits that seem to be the direct expression of an inherited defect. In other Mendelian syndromes, the gene defect results in a preneoplastic state that in turn carries a high risk of cancer; ie, the hamartomatous syndromes. In another group of preneoplastic disorders, the common feature is primary immunodeficiency:X-linked agammaglobulinemia, ataxia telangiectasia, and the Wiskott-Aldrich syndrome. Although the rare hereditary neoplastic syndromes have striking patterns of Mendelian inheritance, the common cancers of man have small familial tendencies. The risk of the same neoplasm developing in a close relative of a cancer patient is about three times greater than would be expected in the general population. Pedigree studies of high-risk families have provided mounting clinical evidence for familial syndromes of multiple cancers. In this connection, familial adenocarcinomatosis and familial cancers of diverse cell types are discussed, along with their relation to multiple primary neoplasia in general. (38 refs.)

77-3694 **Management and Control of Familial Cancer.** (Eng.) Lynch, H. T. (Dept. Preventive Medicine and Public Health, Creighton Univ. Sch. Medicine, Omaha, NB 68178) Lynch, J.; Lynch, P. *Prog Cancer Res Ther* 3: 235-256; 1977.

A discussion is given of improved management and control of familial cancer through the application of family history to the knowledge of cancer genetics and hereditary cancer syndrome identification. One such syndrome is familial breast cancer. Among the eight breast cancer genotypes listed, the site-specific variety is said to account for about one-half of all familial occurrences of this disease. The cancer family syndrome in general is characterized by an excess of adenocarcinomas of all types (particularly those of the colon and endometrium), early age of onset, an excess of multiple primary malignant neoplasms, and a vertical transmission of cancer consistent with an autosomal dominant inheritance pattern. A first-degree relative of a cancer proband from a family manifesting the cancer family syndrome has an approx 50% risk for the development of cancer. Familial occurrences of xeroderma pigmentosum, Sipple's syndrome, and malignant melanoma are also reviewed. The use of the physical or biochemical markers in various syndromes as adjuncts to pedigree methods can single out more specifically those individuals at high risk for cancer. (47 refs.)

77-3695 **Familial Polyposis.** (Eng.) DeCosse, J. J. (8700 W. Wisconsin Ave., Milwaukee, WI 53226) Adams, M. B.; Condon, R. E. *Cancer* 39(1): 267-273; 1977.

Familial polyposis is a genetically transmitted disease characterized by multiple adenomatous colorectal polyps and a high risk for development of single or multiple adenocarcinoma at a young age. Familial polyposis and Gardner's syndrome should be differentiated from other genetically linked polyposis syndromes lacking a predisposition for cancer. Total colectomy and ileorectal anastomosis, aggressive follow-up, and intensive surveillance of asymptomatic relatives can reduce the cancer risk. From an epidemiologic point of view, polyposis is a valuable model for studying the interaction of genetic and environmental factors in the genesis of colon cancer. (54 refs.)

77-3696 **Genetics and Cancer of the Gastrointestinal System.** (Eng.) Dodd, G. D. (Dept. Diagnostic Radiology, Univ. Texas System Cancer Center, M. D. Anderson Hosp. and Tumor Inst., Houston, TX 77030) *Radiology* 123(2): 263-275; 1977.

Gastrointestinal cancers associated with a genetic predisposition include carcinomas of the esophagus, colon, and pancreas, and the polyposis syndromes. Pedigrees for these familial carcinomas are also given. (62 refs.)

77-3697 **Epidemic Lung Cancer in Women (Letter to Editor).** (Eng.) Meigs, J. W. (Connecticut Cancer Epidemiology Unit, New Haven, CT) *JAMA* 238(10): 1055; 1977.

The increase in the number of female cigarette smokers has resulted in an associated drop in the male/female ratio of lung cancer incidence from a peak of 4.7:1 between 1945 and 1949 to 1.9:1 between 1970 and 1974 among persons 35-44 yr old. (7 refs.)

77-3698 **Diet and Cancer.** (Eng.) Lowenfels, A. B. (Dept. Surgery, Westchester County Medical Coll., Valhalla, NY 10595) Anderson, M. E. *Cancer [Suppl]* 39(4): 1809-1814; 1977.

There is a positive correlation between food patterns and cancer incidence in various parts of the world, particularly in the case of gastric and colonic neoplasms. The roles of caloric intake, nutritional content, natural carcinogens, vitamins and alcoholic beverages are also considered. (53 refs.)

77-3699 **Diet, DDT, and the Toxicity of Drugs and Chemicals.** (Eng.) McLean, A. E. (Lab. Toxicology and Pharmacokinetics, Univ. Coll Hosp. Medical Sch., London WC1E 6JJ, England) *Fed Proc* 36(5): 1688-1691; 1977.

The influence of diet on the effects of a carcinogen, drug, or chemical is so profound that dietary alterations could enhance or prevent reaction to the chemical. Toxicity assessments that do not consider nutritional variables may not be correct. (45 refs.)

77-3700 **Dietary Fibre in Scandinavia (Letter to Editor).** (Eng.) Heaton, K. W. (Dept. Medicine, Bristol Royal Infirmary, Bristol BS2 8HW, England) *Lancet* 2(8034): 407-408; 1977.

Lack of dietary fiber is associated with an increased risk of colorectal cancer, and the cancer patients tend to be overweight. A recent study in Scandinavia should be reviewed to determine if the low risk group had less obesity that those persons at risk. (3 refs.)

77-3701 **Current Concepts in Nutrition. Food Additives.** (Eng.) Jukes, T. H. (Div. Medical Physics, Univ. California, Berkeley, CA 94720) *New Engl J Med* 297(8): 427-430; 1977.

Several types of common controversial food additives, including the nitrates and nitrites used in meats, are reviewed with respect to their individual toxicity and/or carcinogenicity. (5 refs.)

77-3702 **Nutritional Factors in the Etiology of Gastro-Intestinal Cancer.** (Eng.) Modan, B. (Dept. Clinical Epidemiology, Chaim Sheba Medical Center, Tel Hashomer and Tel Aviv Univ. Medical Sch., Israel) *Med Biol Environ* 4(1): 3; 1976.

Case control studies in Israel indicate a higher consumption of starches among patients with gastric cancer and a lower fiber consumption among those with colon cancer. However, no single dietary factor can be incriminated in carcinogenesis without a better understanding of metabolic pathways. (no refs.)

77-3703 **Evaluation of Six Short Term Tests for Detecting Organic Chemical Carcinogens and Recommendations for Their Use.** (Eng.) Purchase, I. F. (Imperial Chemical Industries Ltd., Central Toxicology Laboratory, Alderley Park, Cheshire, England) Longstaff, E.; Ashby, J.; Styles, J. A.; Anderson, D.; Lefevre, P. A.; Westwood, F. R. *Nature* 264(5587): 624-627; 1976.

One hundred twenty organic compounds (58 known carcinogens) were subdivided into four broad chemical classes and were subjected to six short-term tests for potential carcinogenicity: (1) Ames test, (2) cell transformation, (3) Rabin's test, (4) sc implants, (5) sebaceous gland test and (6) tetrazolium reduction test. The percentage of correct predictions made by each test for the different classes revealed that tests 1 and 2 performed well with all classes (polycyclics, arylamines, alkylating agents, and miscellaneous compounds); test 4 responded well to alkylating agents; and test 5 responded well to polycyclic aromatic hydrocarbons. Basing an assessment on the number of false positives produced, tests 1 and 2 were again more reliable than the other tests. The Ames test gave 91% accuracy for 52 carcinogens and 93% accuracy for 62 noncarcinogens, while the respective values for the cell transformation test were 91% and 97%. For carcinogens and noncarcinogens the accuracy of Rabins test was 71 and 71%, of sc implants, 37 and 95%, of sebaceous gland suppression, 67 and 64%, and of tetrazolium reduction, 40 and 73%. A further assessment of the capability of each test to distinguish correctly between the eight structurally related carcinogen and noncarcinogen pairs underlined the relative reliability of tests 1 and 2. Test 1 correctly distinguished between all eight pairs, and test 2 distinguished between seven pairs; the other tests ranged between two and five correct predictions. Although these short-term tests have been of value in research and screening programs, the possibility of a large proportion of false positives is a drawback. A system of preselection based on structural analogies between untested compounds and established carcinogens is suggested before screening, ie class-specific as well as test-specific control pairs. Care will have to be taken to select and screen representatives of new or previously untested chemical classes. (18 refs.)

77-3704 **Sister Chromatid Exchange and Chromosome Aberration Analysis with the Use of Several Carcinogens and Noncarcinogens: Brief Communication.** (Eng.) Popescu, N. C. (Biology Branch, Carcinogenesis Program, NCI, NIH, Public Health Service, U.S. Dept. Health, Education and Welfare, Bethesda, MD 20014) Turnbull, D.; DiPaulo, J. A. *J Natl Cancer Inst* 59(1): 289-293; 1977.

Several chemical carcinogens and noncarcinogens were tested for their ability to induce sister chromatid exchanges (SCE) and structural chromosome aberrations in cultured V79-4 Chinese hamster cells. All direct-acting carcinogens, ie, N-methyl-N′-nitro-N-nitrosoguanidine, N-acetoxyfluorenylacetamide, N-hydroxyfluorenylacetamide, and 4-nitroquinoline-1-oxide, induced a large increase in SCE frequency. Proflavine and acridine orange, which are mutagenic in microorganisms but not (or putatively weakly) carcinogenic in vivo, also increased the frequency of SCE. Three carcinogenic polycyclic hydrocarbons, benzo(a)pyrene, 3-methylcholanthrene, and 7,12-dimethylbenz(a)anthracene, increased the incidence of SCE only when a metabolizing feeder layer was used. No increase was observed with two noncarcinogenic hydrocarbons, pyrene and phenanthrene, tested under similar conditions. The other noncarcinogens (hydroxyurea, methylene blue, perylene) did not influence SCE frequency. Although some chemicals increased the frequency of structural chromosome aberrations, no correlation was found between the frequencies of SCE and the aberrations. (32 refs.)

77-3705 **Aflatoxin B-Oxide Generated by Chemical or Enzymic Oxidation of Aflatoxin B_1 Causes Guanine Substitution in Nucleic Acids.** (Eng.) Martin, C. N. (Cancer Res. Unit, Univ. York, Heslington, Yorkshire, England) Garner, R. C. *Nature* 267(5614): 863-865; 1977.

The generation of aflatoxin B_1 8,9-oxide by the peracid oxidation of aflatoxin B_1 (AFB_1) is reported. Using a modified chemical procedure, AFB_1 was covalently bound to DNA, polyguanylic acid, or deoxyguanosine. Enzymatic binding was achieved by incubating AFB_1 with rat liver postmitochondrial supernatants and DNA, together with the necessary cofactors. Enzymatic hydrolysis or acid hydrolysis of the DNA or polyguanosine to which AFB_1 had been bound led to the release of AFB_1 8,9-dihydrodiol, indicating that AFB_1-8,9-oxide was formed by either enzymatic or chemical oxidation of AFB_1. Two major products were formed by the peracid oxidation, and both were derived from guanine, probably through N-7 substitution. Covalent binding of AFB_1 with guanine at the N-7 position is likely to induce frame-shift mutations due to intercalation of the AFB_1 molecule together with base-substitution mutations as a result of misrepair. The results indicated that AFB_1-8,9-oxide is formed during the peracid oxidation of AFB_1 and that this metabolite reacts with nucleic acid. (14 refs.)

7-3706 **Carbohydrate Metabolism in Aflatoxin Toxicity.** (Eng.) Jayanthi Bai, N. (Dept. Biochemistry, '. D. Medical Coll., Alleppey 688 005, India) Ramachandra 'ai, M.; Venkitasubramanian, T. A. *Indian J Biochem Biohys* 14(1): 86-88; 1977.

'he effects of aflatoxins B_1, G_1, and M_1 on carbohydrate meabolism in rat liver and kidney were studied 48 hr after the › injection of single LD50 doses of the toxins. The aflatoxins ailed to elicit any significant changes in hepatic glycogen evel, but they increased phosphofructokinase activity in both he liver and kidneys. Pyruvate kinase activity was nhibited by aflatoxin M_1 in both tissues. Liver gluose-6-phosphatase activity was reduced by aflatoxin B_1 and flatoxin G_1, but the kidney enzyme was not affected. \flatoxin M_1 increased the activity of this enzyme in the kidey, but did not affect it in the liver. Aflatoxins B_1 and G_1 nhanced the activity of hexose monophosphate dehydrogeiase in both tissues, but M_1 enhanced it in the kidney but not n the liver. The results indicate that carbohydrate metaboism is affected differently by these toxins. (21 refs.)

77-3707 **The Effect of Functional Groups on the Interaction of Aflatoxins B_1 and G_1 with Starch, Cellulose, and Seven Cellulose Derivatives.** (Eng.) Uwaifo, A. O. (Dept. Biochemistry, Univ. Ibadan, Ibadan, Nigeria) Bassir, O. *Biochem Pharmacol* 26(9): 863-866; 1977.

The interaction of several polysaccharides with aflatoxin B_1 and aflatoxin G_1 was studied by equilibrium dialysis to determine the effects of different functional groups on binding. Polysaccharides were chosen as macromolecular models because the glucose chain is basically a constant moiety in their structure, and any differences in their interaction would be due to the functional groups. The results showed a marked variation in binding. No binding was observed with cellulose, carboxymethyl cellulose, phosphocellulose, and cellulose acetate. However, the amino derivatives of cellulose--ECTEOLA cellulose, triethylaminoethyl cellulose, and diethylaminoethyl cellulose--bound the aflatoxins. In general, aflatoxin B_1 bound more strongly to the polysaccharides than aflatoxin G_1. (18 refs.)

77-3708 **Diurnal Oscillation of Rat Liver Mediated Mutagenesis by Aflatoxin B_1 (Meeting Abstract).** (Eng.) Pariza, M. W. (Food Res. Inst., Dept. Food Microbiology and Toxicology, Univ. Wisconsin, Madison, WI 53706) Rappaport, H.; Garcia, V. M.; Geopfert, J. M. *Proc Am Assoc Cancer Res* 18: 26; 1977. (no refs.)

77-3709 **Studies on an Aflatoxin-Guanine Adduct Produced In Vitro and In Vivo in DNA (Meeting Abstract).** (Eng.) Essigmann, J. M. (MIT, Cambridge, MA 02139) Croy, R. G.; Busby, W. F. *Proc Am Assoc Cancer Res* 18: 179; 1977. (no refs.)

77-3710 **Oncogenic and Mutagenic Activity of Adriamycin Decreased by Microsomal Metabolism (Meeting Abstract).** (Eng.) Marquardt, H. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021) Baker, S.; Grab, D. *Proc Am Assoc Cancer Proc* 18: 13; 1977. (no refs.)

77-3711 **Mutagenic Activity of Quercetin and Related Compounds.** (Eng.) Bjeldanes, L. F. (Dept. Nutritional Sciences, Univ. California, Berkeley, CA 94720) Chang, G. W. *Science* 197(4303): 577-578; 1977.

The mutagenicity of several flavonoids and flavonoid metabolites to *Salmonella typhimurium* strains TA1538 and TA98 (sensitive to frameshift mutations) and TA1535 and TA100 (sensitive to base-pair substitutions) was estimated. The test compounds were naringin, rutin, neohesperetin, hesperetin, dihydroquercetin, quercetin, quercetin pentaacetate, permethylquercetin, m-hydroxyphenylacetic acid, and m,p-dihydroxyphenylacetic acid. Of these compounds, only quercetin was mutagenic (to TA98 and TA1538) without metabolic activation. With activation, the mutagenic activity of quercetin was increased, and the mutagenicity of quercetin pentaacetate to TA98, TA100, and TA1538 was revealed. The mutagenic activity of quercetin was from one to three orders less than that of the potent mutagens aflatoxin B_1 and 2-aminofluorene. Quercetin occurs widely in foods such as fruits, vegetables, and tea, and its mutagenic and carcinogenic potential should be investigated further. (11 refs.)

77-3712 **Effects of Phorbol Esters on DNA Synthesis in C3H/10T1/2 Mouse Fibroblasts (Meeting Abstract).** (Eng.) Peterson, A. R. (McArdle Lab., Univ. Wisconsin, Madison, WI 53706) Heidelberger, C. *Proc Am Assoc Cancer Res* 18: 18; 1977. (no refs.)

77-3713 **Tumor-Promoting Activity of 2,3-Dihydrophorbol Myristate Acetate in Mouse Skin (Meeting Abstract).** (Eng.) Segal, A. (Lab. Organic Chemistry and Carcinogenesis, Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY 10016) Van Duuren, B. L.; Mate, U. *Proc Am Assoc Cancer Res* 18: 21; 1977. (1 ref.)

77-3714 **Calcium Ion Effects in the Binding of Phorbol Myristate Acetate to Rat Liver Plasma Membranes (Meeting Abstract).** (Eng.) Witz, G. (Lab. Organic Chemistry and Carcinogenesis, Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY 10016) Van Duuren, B. L. *Proc Am Assoc Cancer Res* 18: 34; 1977. (no refs.)

77-3715 **Vitamin A Acid (Retinoic Acid), A Potent Inhibition of 12-O-Tetradecanoyl-Phorbol-13-Acetate (TPA)-Induced Ornithine Decarboxylase (ODC) Activity in Mouse Epidermis (Meeting Abstract).** (Eng.) Verma, A. K. (McArdle Lab., Univ. Wisconsin, Madison, WI 53706) Holder, J. W.; Boutwell, R. K. *Proc Am Assoc Cancer Res* 18: 14; 1977. (no refs.)

77-3716 **Effects of 12-O-Tetradecanoyl-Phorbol-13-Acetate on Cloning Efficiency, DNA Synthesis and Transformation of Hamster Embryo Cells (Meeting Abstract).** (Eng.) Poiley, J. A. (NCI Frederick Cancer Res. Center, Frederick, MD 21701) *Proc Am Assoc Cancer Res* 18: 14; 1977. (no refs.)

77-3717 **Polyamines as Mediators of Tumor Promotion (Meeting Abstract).** (Eng.) Lichti, U. (NCI, Bethesda, MD 20014) Yuspa, S.; Ben, T.; Patterson, E.; Slaga, T. *Proc Am Assoc Cancer Res* 18: 65; 1977. (no refs.)

77-3718 **Absence of Modification of Oestrogen Receptivity in Rat Mammary Tissue after 7,12-Dimethylbenz[a]anthracene Administration.** (Eng.) Leclercq, G. (Service de Medecine, Institut J. Bordet, B-1000 Brussels, Belgium) Devleeschouwer, N.; Deboel, M. C.; Heuson, J. C. *Arch Int Physiol Biochim* 85(1): 181-183; 1977.

In Sprague-Dawley rats fed 20 mg 7,12-dimethylbenz[a]anthracene, there were no significant changes in the binding affinity of mammary cytoplasmic estrogen receptors, nor did massive derepression of estrogen receptor synthesis occur in most cells. (4 refs.)

77-3719 **Effect of High Fat Diet on Serum Prolactin Levels and Mammary Cancer Development in Ovariectomized Rats (Meeting Abstract).** (Eng.) Chan, P. C. (American Health Foundation, Valhalla, NY 10595) Head, J. F.; Cohen, L. A.; Wynder, E. L. *Proc Am Assoc Cancer Res* 18: 189; 1977. (no refs.)

77-3720 **Guanosine (G) and 7,12-Dimethylbenz(a)-anthracene 5,6-Oxide (DMBA Oxide) and Comparison to RNA Adducts Formed in Tissue Culture (Meeting Abstract).** (Eng.) Frenkel, K. (Columbia Univ., New York, NY 10032) Grunberger, D.; Tanis, S.; Nakanishi, K. *Proc Am Assoc Cancer Res* 18: 114; 1977. (no refs.)

77-3721 **Changes in the Metabolism of 7,12-Dimethylbenz(a)anthracene under the Influence of Vitamin A.** (Rus.) Khandudzha, K. L. (M. V. Lomonsov Moscow State Univ., Moscow, USSR) Esakova, T. D.; Semin, B. K.; Petrusevich, Yu. M.; Tarusov, B. N. *Biull Eksp Biol Med* 83(5): 579-582; 1977.

The in vitro metabolism of 7,12-dimethylbenz(a)anthracene (DMBA) upon incubation with liver microsomes and with liver and mammary gland homogenates from rats fed a vitamin A-enriched diet was studied. Vitamin A inhibited the formation of water-soluble metabolites. The amount of lipophilic metabolites extracted from the microsomes and from the liver and mammary gland homogenates was decreased by a factor of 2.2 and 5, respectively. The amount of unmetabolized DMBA in the liver microsomes was the same in control and experimental animals. (16 refs.)

77-3722 **Transplacental Carcinogenesis by DMBA in Hamsters (Meeting Abstract).** (Eng.) Rustia, M. (Eppley Inst. Res. Cancer, Omaha, NB 68105) *Proc Am Assoc Cancer Res* 18: 1; 1977. (no refs.)

77-3723 **Inverse Correlation Between Species Life Span and Capacity of Cultured Fibroblasts to Bind 7,12-Dimethylbenz(a)anthracene to DNA (Meeting Abstract).** (Eng.) Schwartz, A. G. (Fels Res. Inst. and Dept. Microbiology, Temple Medical Sch., Philadelphia, PA 19140) Moore, C. J. *Proc Am Assoc Cancer Res* 18: 36; 1977. (1 ref.)

77-3724 **Poly(a) RNA Concentrations in Rat Mammary Epithelial Cells During DMBA-Induced**

Tumorigenesis (Meeting Abstract). (Eng.) DeAngelo, A. B. (NCI, Frederick Cancer Res. Center, Frederick, MD 21701) Mohan, F. P. *Proc Am Assoc Cancer Res* 18: 35; 1977. (1 ref.)

77-3725 **Genetic Differences in Mouse Ovarian Metabolism of 3-Methylcholanthrene and Oocyte Toxicity.** (Eng.) Mattison, D. R. (Section Molecular Toxicology, Developmental Pharmacology Branch, Natl. Inst. Child Health and Human Development, NIH, Bethesda, MD 20014) Thorgeirsson, S. S. *Biochem Pharmacol* 26(9): 909-912; 1977.

The ovarian metabolism of 3-methylcholanthrene (3-MC) by aryl hydrocarbon hydroxylase (AHH) and changes in oocyte number after 3-MC treatment were investigated in C57BL/6N (B6) and DBA/2N (D2) mice. These strains were chosen because they differ in AHH induction after treatment with polycyclic aromatic hydrocarbons (PAH): B6 mice, homozygous for the Ah-b locus, produce a severalfold increase in AHH activity after PAH treatment, but D2 mice, homozygous for the Ah-d locus, do not. Six-week-old mice were given a single ip dose of 80 mg/kg 40 hr prior to sacrifice. Ovarian AHH activity was increased threefold in the B6 ovary, but no increase was found in the D2 ovary. Experiments with genetic crosses between these two strains suggest that this induction of ovarian AHH activity segregates as an autosomal dominant trait. The different metabolic rates and profiles of PAH could lead to differences in the kind and degree of toxicity. To determine if the difference in AHH induction in response to 3-MC was accompanied by differences in the rate of primordial oocyte destruction, the same dose of 3-MC was given to 4-wk-old mice. Upon sacrifice 1 wk later, 97% of the primordial oocytes in the responsive B6 mice were destroyed, compared to only 50% of the oocytes in the nonresponsive D2 strain. The striking concordance of increased ovarian AHH activity and oocyte destruction in the B6 mouse suggests that oocyte destruction is mediated by the formation of one or more toxic metabolites, which are formed more rapidly in B6 mice than in D2 mice. (9 refs.)

77-3726 **Comparative Carcinogenicity of Benzo(a)pyrene and 3-Methylcholanthrene Derivatives and Parent Compounds with Implications on the Mechanism of Tumor Initiation (Meeting Abstract).** (Eng.) Cavalieri, E. (Eppley Inst., Univ. Nebraska Medical Center, Omaha, NE 68105) Althoff, J.; Grandjean, C. *Proc Am Assoc Cancer Res* 18: 59; 1977. (no refs.)

77-3727 **Induction of Squamous Cell Carcinoma in the Lung of C57BL/6 Mice by Intratracheal Instillation of Benzo(a)pyrene with Charcoal Powder.** (Eng.) Yoshimoto, T. (Third Dept. Internal Medicine, Osaka Univ. Medical Sch., Fukushima 1-1-50, Fukushima-ku, Osaka 553, Japan) Hirao, F.; Sakatani, M.; Nishikawa, H.; Ogura, T.; Yamamura, Y. *Gann* 68(3): 343-352; 1977.

Repeated intratracheal instillations of benzo(a)pyrene (1.0 mg) with charcoal powder (0.5 mg) suspended in saline solution readily induced squamous cell carcinomas in the lungs of C57BL/6 mice. Intratracheal instillations were performed once a week for 8 wk, and the observation period was 40 wk. Highly keratinized and moderately keratinized squamous cell carcinomas occurred. At a later period of observation, poorly differentiated squamous cell carcinomas were also found. Invasion into blood vessels was occasionally seen, but metastasis to regional lymph nodes or distant metastasis was not found. One tumor from a mouse killed on the 280th day was successfully transplanted sc into a syngeneic mouse. This animal, killed on the 84th day after the first transplantation, had a pulmonary metastasis. (19 refs.)

77-3728 **Benzo(a)pyrene-induced Early Alterations of the Respiratory Epithelium in the Syrian Golden Hamster.** (Eng.) Mohr, U. (Abteilung fur Experimentelle Pathologie, Medizinische Hochschule Hannover, 3000 Hannover 61, Karl-Wiechert-Allee 9, W. Germany) Reznik-Schuller, H. *IARC Sci Publ* (16): 89-97; 1977.

Alterations occurring in the epithelia of the trachea and the lobar and segmental bronchi of female Syrian golden hamsters during a 20-wk period of weekly benzo(a)pyrene (BP, 0.63 mg) administration were examined by light and electron microscopy. The first alteration was detected in both the tracheal and bronchial epithelia around the fourth week, and it consisted of an occasional slight proliferation of basally situated cells. During the following weeks, pronounced hyperplasia developed in the trachea. The first morphologically detectable signs of a keratin synthesis took place about the 13th week. A marked stratification of the hyperplastic and metaplastic epithelia was also noticeable in the trachea. The bronchial epithelial cells showed no signs of keratinization, indicating that BP did not induce squamous cell metaplasia in this part of the respiratory system. Hyperplasia was less pronounced here than in the trachea, and there was no epithelial stratification. Small adenomas developed, but there was no squamous metaplasia. These results demonstrate that the site of origin greatly influences the mode of neoplastic development in the respiratory system. Although induced by the same carcinogen, the pathological alterations that occurred in tracheal and bronchial epithelia differed markedly. (8 refs.)

77-3729 **Binding of Benzo(a)pyrene (BP) to Human Bronchial Biopsy Fragments in Short-term Organ Culture (Meeting Abstract).** (Eng.) Genta, V. (Univ.

South Florida, Tampa, FL 33612) Cavaliere, S.; Antonini, A. *Proc Am Assoc Cancer Res* 18: 17; 1977. (no refs.)

77-3730 **Benzo(a)pyrene Metabolism in Human Monocytes (Meeting Abstract).** (Eng.) Lake, R. S. (Children's Hosp. Akron, Akron, OH 44308) Freeman, A. E.; Igel, H. J. *Proc Am Assoc Cancer Res* 18: 32; 1977. (no refs.)

77-3731 **Structures of Nucleic Acid Adducts Formed in Human Bronchial Explants Exposed to Benzo(a)pyrene (Meeting Abstract).** (Eng.) Jeffrey, A. M. (Columbia Univ., New York, NY 10032) Grzeskowiak, K.; Jennette, K. W.; Weinstein, I. B.; Harris, C.; Harvey, R. G. *Proc Am Assoc Cancer Res* 18: 180; 1977. (no refs.)

77-3732 **Conformation and Template Properties of DNA Modified with a Dihydrodiol Epoxide of Benzo(a)pyrene (BP) (Meeting Abstract).** (Eng.) Pulkrabeck, P. (Columbia Univ., New York, NY 10032) Leffler, S.; Grunberger, D.; Weinstein, I. B. *Proc Am Assoc Cancer Res* 18: 179; 1977. (no refs.)

77-3733 **Evidence of Excision Repair in Human Cells of DNA Damage Caused by the 7,8-Dihydrodiol-9,10-oxide ("Anti" Isomer) and the 4,5-Oxide of Benzo(a)pyrene (Meeting Abstract).** (Eng.) McCormick, J. J. (Michigan State Univ., East Lansing, MI 48824) Heflich, R. H.; Maher, V. M. *Proc Am Assoc Cancer Res* 18: 190; 1977. (no refs.)

77-3734 **Nuclear Metabolism of Benzo(a)pyrene (BP) and of (±)Trans 7,8-Dihydroxy-7,8-Dihydro-BP: Chromatographic Analysis of Aralkylated DNA (Meeting Abstract).** (Eng.) Bresnick, E. (Univ. Vermont, Burlington, VT) Vaught, J. B.; Thakker, D. R.; Jerina, D. M.; Stoming, T. A. *Proc Am Assoc Cancer Res* 18: 33; 1977. (no refs.)

77-3735 **Role of Volcanoes in the Formation of Carcinogenic Substances.** (Rus.) Il'nitskii, A. P. (Oncological Scientific Center, Acad. Medical Sciences USSR, Moscow, USSR) Gvil'dis, V. Iu.; Mishchenko, V. S.; Shabad, L. M. *Dokl Akad Nauk SSSR* 234(3): 717-719; 1977.

The content of benzo(a)pyrene (BP) in the lava and ashes of the Kamchatka and Chukotski peninsula volcanos (USSR) was studied by fluorescence spectrometry. The BP content in the volcanic outbursts varied from 0.3 to 5.4-6.1 μg/kg. Thus, the annual amount of volcanic BP produced may be as great as several tons. (12 refs.)

77-3736 **Effects of Inducers and Inhibitors of the Benzo(a)pyrene Hydroxylase of Isolated Rat Liver Nuclei and Nuclear Envelopes on the Binding of Benzo(a)pyrene to DNA.** (Eng.) Alexandrov, K. (Institut de Recherches Scientifiques sur le Cancer, B.P. 8, 94800-Villejuif, France) *Eur J Cancer* 13(8): 847-853; 1977.

Liver nuclei from rats pretreated with different inducers of mixed function oxidases were incubated with ^{3}H-benzo(a)pyrene (^{3}H-BP). The binding of ^{3}H-BP to nuclear DNA increased after induction by 3-methylcholanthrene (3-MC), but not after pretreatment of rats with phenobarbital (PB) or pregnenolone 16α-carbonitrile. 7,8-Benzoflavone (7,-8-BF), a known inhibitor of aryl hydrocarbon hydroxylase, inhibited the binding of ^{3}H-BP to DNA by about 80% in nuclei from 3-MC-pretreated rats but not in nuclei from PB-pretreated or control rats. While 1,1,-trichloropropene 2,3-oxide (TCPO), an inhibitor of PB epoxide hydratase, was added to the nuclei, the binding of ^{3}H-BP to DNA increased in the nuclei of both untreated and treated rats. Microsomes from 3-MC-pretreated rats, when added to the nuclei, increased the binding two- to fivefold. A slight decrease in binding occurred when control microsomes were incubated with nuclei from 3-MC-pretreated rats, compared with the same incubation without microsomes. In experiments with denuded nuclei, the addition of nuclear membranes to the medium increased the binding only when the membranes were from 3-MC-pretreated rats. The effect of added 7,8-BF or TCPO to the medium was similar to that observed with intact nuclei. These latter results show that the enzyme activity that activated BP to species that bind to DNA is located in the nuclear envelope. (19 refs.)

77-3737 **Aryl Hydrocarbon Hydroxylase Activity in the Liver of Genetically Different Mouse Lines During Chemical Carcinogenesis.** (Rus.) Rivkind, N. B. (Inst. Clinical and Experimental Medicine, Siberian Branch, Acad. Sciences USSR, Novosibirsk, USSR) Tsyrlov, I. B.; Liakhovich, V. V. *Dokl Akad Nauk SSSR* 234(1): 231-234; 1977.

Carcinogenic polycyclic hydrocarbons (PH) induce, in the livers of mice de novo synthesis of aberrant cytochrome P-448, which in turn hydroxylates PC molecules. Genetic matings between DBA/2 mice, resistant to this induction, and C57BL/6 mice sensitive to this induction, showed that the induction trait is inherited as a simple autosomal dominant character. To determine whether high concentrations of benzo(a)pyrene (BP) can induce aryl hydrocarbon hydroxylase (AHH) activity, C57BL/6, DBA/2, and (C57BL/6 x DBA/2)F$_1$ mice were treated with 20 μg/kg BP, 2x/wk, for 10-22 wk. Cytochrome P-448 levels reached a max on days 4-14 after BP administration in C57BL/6 and (DBA/2 x C57BL/6) mice, but DBA/2 mice showed only slight elevation of enzymatic activity on days 14-20, which reflects the slight induction of P-448 after prolonged exposure to high concentrations of BP in these mice. (15 refs.)

77-3738 **Investigation on the Carcinogenic Burden by Air Pollution in Man. XV. Polycyclic Aromatic Hydrocarbons in Automobile Exhaust Gas--An Inventory.** (Eng.) Grimmer, G. (Biochemisches Institut fur Umweltcarcinogene, Sieker Landstr, 19, D-2070 Ahrensburg, W. Germany) Bohnke, H.; Glaser, A. *Zentralbl Bakteriol [Orig B]* 164(3): 218-234; 1977.

Polycyclic aromatic hydrocarbons (PAH) emitted by two different engines were separated by gas chromatography and characterized by mass spectrometry (MS) after enrichment from an exhaust gas condensate. Gasoline was also investigated with this technique. The quantities of PAH with boiling points > 338 C in the exhaust gas and in the fuel were compared. Of the approx 150 different PAH characterized by MS, 75 were identified by comparison with authentic samples. Six PAH compounds, consisting of four to seven rings and suspected of possessing carcinogenic activity, are described for the first time. The MS and UV spectral data support the proposed structures of the previously identified PAH (11H-cyclopenta(qrs)benzo(e)pyrene, 10H-cyclopenta-(mno)benzo(a)pyrene, benzo (ghi)cyclopenta(pqr)-perylene, cyclopentenopyrene). The different PAH profiles of the fuel and the exhaust gas lead to the conclusion that most or all PAH of the fuel are combusted and that the PAH emitted are formed de novo during combustion. (13 refs.)

77-3739 **Oncogenic Interaction of Carcinogenic and Non-carcinogenic Polycyclic Aromatic Hydrocarbons in Mice.** (Eng.) Pfeiffer, E. H. (Hygiene-Institut der Universitat Mainz, 65 Mainz, Hochhaus am Augustusplatz, W. Germany) *IARC Sci Publ* (16): 69-77; 1977.

The carcinogenicity of 12 polycyclic aromatic hydrocarbons (PAH) occurring in automobile exhaust condensates, either alone or in combination, was tested in 3,000 female NMRI mice. Six different doses of benzo(a)pyrene (BP, 3-100 μg) and of dibenzo(a,h)anthracene (DBA, 2-75 μg) and mixtures of the two were tested sc. Mixtures of 10 noncarcinogenic hydrocarbons were also tested: benzo(e)pyrene, benzo(a)anthracene, phenanthrene, anthracene, pyrene, fluoranthene, chrysene, perylene, benzo(ghi)perylene, and coronene. All 12 PAH were also applied in combination in ratios calculated from analyses of exhaust condensates derived from the Europa motorcycle. All mice were palpated for developing tumors at weekly intervals until the end of the 114th wk after treatment, when the experiment was terminated. Small doses of DBA had a greater tumor-promoting effect than did comparable of BP. Increased doses increased the effect of BP more than that of DBA. BaP + DBA was 1.4 times more active than DBA alone. The mixture of all PAH had a lower efficacy than DBA alone. It is concluded that tumor formation after the application of DBA together with the 10 noncarcinogenic hydrocarbons is predominantly induced by DBA, with no essential influence of BP or the other 10 PAH. (15 refs.)

77-3740 **Carcinogen Metabolism in Human Liver, Normal and Tumorous Lung Tissues (Meeting Abstract).** (Eng.) Sabadie, N. (International Agency for Res. on Cancer, Lyon, France) Camus, A.; Malaveille, C.; Richter-Reichhelm, H. B.; Mohr, U.; Bartsch, H. *Proc Am Assoc Cancer Res* 18: 37; 1977. (no refs.)

77-3741 **Strain Differences in Mouse Ovarian Aryl Hydrocarbon Hydroxylase and Ovotoxicity (Meeting Abstract).** (Eng.) Mattison, D. R. (NIH, Bethesda, MD 20014) Thorgeirsson, S. S. *Proc Am Assoc Cancer Res* 18: 18; 1977. (no refs.)

77-3742 **Effect of Cell Age, Serum Concentration and Confluence on the Binding of Polynuclear Aromatic Hydrocarbons to Human Embryo Cell Macromolecules (Meeting Abstract).** (Eng.) Raineri, R. (NCI Frederick Cancer Res., Frederick, MD 21701) Hillesund, T. *Proc Am Assoc Cancer Res* 18: 14; 1977. (no refs.)

77-3743 **Mechanism for the Incorporation of Polycyclic Hydrocarbons Into Protein (Meeting Abstract).** (Eng.) Morrison, W. C. (Dept. Biochemistry, Univ. Tennessee Center Health Sciences, Memphis, TN 38163) Morrison, J. C.; Whybrew, W. D.; Trass, T. C.; Bucovaž, E. T. *Proc Am Assoc Cancer Res* 18: 12; 1977. (no refs.)

77-3744 **Interaction of Polycyclic Hydrocarbons with DNA In Vivo and the Resultant Conformational Changes (Meeting Abstract).** (Eng.) Eastman, A. R. (Univ. Vermont Coll. Medicine, Burlington, VT 05401) *Proc Am Assoc Cancer Res* 18: 33; 1977. (no refs.)

77-3745 **Syncarcinogenesis in Cultured C3H/10T1/2 Cells (Meeting Abstract).** (Eng.) Mondal, S. (McArdle Lab. Cancer Res., Madison, WI 53706) Brankow, D. W.; Heidelberger, C. *Proc Am Assoc Cancer Res* 18: 8; 1977. (no refs.)

77-3746 **The Role of Naphthalenes as Cocarcinogens (Meeting Abstract).** (Eng.) Schmeltz, I. (American Health Foundation, Valhalla, NY) Hilfrich, J.; Tosk, J.; Hoffmann, D.; Wynder, E. L. *Toxicol Appl Pharmacol* 41(1): 156; 1977. (no refs.)

77-3747 **Metabolism and Covalent Binding of [^{3}H]Benzo(a)pyrene by Isolated Perfused Lungs and Short-Term Tracheal Organ Culture of Cigarette Smoke-exposed Rats.** (Eng.) Cohen, G. M. (Dept. Biochemistry, Univ. Surrey, Guildford GU2 5XH, Surrey, England) Uotila, P.; Hartiala, J.; Suolinna, E. M.; Simberg, N.; Pelkonen, O. *Cancer Res* 37(7): 2147-2155; 1977.

The metabolism and covalent binding of the carcinogen benzo(a)pyrene (BP), a constituent of cigarette smoke, was determined in the isolated perfused lungs of sham- and cigarette smoke-exposed and 3-methylcholanthrene (MC)-pretreated male Wistar rats. Rats were exposed to cigarette smoke for 1 hr daily for either 1 or 10 days. BP (2 nanomoles) was instilled intratracheally, and metabolites in the lungs and a nonrecirculating perfusate were determined. BP was metabolized by the isolated perfused lungs of sham-, cigarette smoke-exposed, and MC-treated animals to ethyl acetate-soluble metabolites, which cochromatographed with 9,10-dihydro-9,10-dihydroxybenzo(a)pyrene, 7,8-dihydro-7,8-dihydroxybenzo(a)pyrene, 4,5-dihydro-4,5-dihydroxybenzo(a)pyrene and 3-hydroxybenzo(a)pyrene. An unidentified metabolite (γ) migrating between 4,5-dihydro-4,5-dihydroxybenzo(a)pyrene and 3-hydroxybenzo(a)pyrene was observed in the lung perfusates from animals that had been exposed either to cigarette smoke or MC. Metabolite production was significantly increased by exposure to either cigarette smoke or MC. Tracheas of sham- and smoke-exposed animals also converted BP to metabolites that cochromatographed with reference dihydrodiols and 3-hydroxybenzo(a)pyrene; however, no increase in metabolite production was observed in the smoke-exposed animals. Dihydrodiols were the major ethyl acetate-soluble metabolites formed by the trachea, whereas 3-hydroxybenzo(a)pyrene was the major metabolite formed in the lung perfusates. After intratracheal instillation of ^{3}H-BP, the amount of covalently bound radioactivity was significantly increased in the lungs of animals exposed to cigarette smoke compared with the corresponding sham-exposed animals. (34 refs.)

77-3748 **Inhalation Toxicity Studies on Cigarette Smoke. IV. Expression of the Dose of Smoke Particulate Material Applied to the Lungs of Experimental Animals.** (Eng.) Binns, R. (Group Res. and Development Centre, British-American Tobacco Co. Limited, Regents Park Road, Southampton, Hants, England) *Toxicology* 7(2): 189-195; 1977.

Total particulate matter (TPM) doses applied to the lungs of animals were calculated from experimental dosimetry data. The TPM levels achieved in several species following smoke exposure were related to body wt, lung wt, and alveolar surface areas. The dose levels in animals were compared with estimates of the TPM dose that might be retained by a human cigarette smoker. Cigarette dosage equivalents to which animals are subjected can be calculated on the basis of these comparisons. The validity of making extrapolations from animal dosimetry data to the human exposure situation is questioned. (18 refs.)

77-3749 **Experimental Investigations on the Tumorigenic Activity of Cigarette Smoke Condensate on Mouse Skin. VII. Comparative Studies of Condensates from Different Modified Cigarettes.** (Ger.) Dontenwill, W. (Agathe-Lasch-Weg 25, D-2000 Hamburg 52, W. Germany) Chevalier, H. J.; Harke, H. P.; Klimisch, H. J.; Reckzeh, G.; Fleischmann, B.; Keller, W. *Z Krebsforsch* 89(2): 145-151; 1977.

Condensates from different modified cigarettes were compared with condensates from standard cigarettes with regard to their tumorigenic activity on mouse skin. Significantly lower effects were observed in test series with cigarettes from expanded tobacco. Different results were obtained in experiments with cigarettes from new smoking materials. In one case the effect was higher; in two other cases the effect was lower in comparison to the effect of condensate from reference cigarettes. The diameter of the cigarette may have some influence; ie, thinner cigarettes had a lower biological effect. The lowest tumorigenic effect was observed in tests of cigarettes with a high content of Burley stems. (4 refs.)

77-3750 **The Carcinogenic Effect of Cigarette Smoke: The Effect of Cigarette Smoke on Human Gas-**

tric Mucosal Cells in Organ Culture. (Eng.) Tayler, R. (Dept. Medicine, Royal North Shore Hosp. Sydney, St. Leonards, New South Wales 2065, Australia) Piper, D. W. *Cancer* 39(6): 2520-2523; 1977.

The effect of cigarette smoke condensate (CSC, 0.10 mg/ml) on gastric mucosa grown in organ culture was compared with that of the known gastric carcinogen N-methyl-N′-nitro-N-nitrosoguanidine (MNNG, 0.75 mM). Tissues from 10 patients with chronic peptic ulcer or gastric adenocarcinoma were used. Both CSC and MNNG caused a small but significant decrease in cell viability, as measured by incorporation of labeled glucose and glycine. As judged by lactate and 3-glucuronidase production in the ambient fluid, CSC produced a metabolic response similar to that induced by MNNG. The results indicate that CSC, like MNNG, has a toxic and carcinogenic effect on gastric mucosal cells. (55 refs.)

77-3751 **Early Proliferative Changes in Rat Pyloric Mucosa Induced with N-Methyl-N-Nitro-N-Nitroso-Guanidine (MNNG) (Meeting Abstract).** (Eng.) Deschner, E. E. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021) Tamura, K.; Bralow, S. P. *Proc Am Assoc Cancer Res* 18: 239; 1977. (no refs.)

77-3752 **Effect of Prolonged Administration of Gastrin on Experimental Carcinogenesis in Rat Stomach Induced by N-Methyl-N′-nitro-N-nitrosoguanidine.** (Eng.) Tatsuta, M. (Dept. Gastroenterology, Center for Adult Diseases, Osaka, 3-3 Nakamichi 1-chome, Higashinari-ku, Osaka 537, Japan) Itoh, T.; Okuda, S.; Taniguchi, H.; Tamura, H. *Cancer Res* 37(6): 1808-1810; 1977.

The effects of prolonged gastrin administration on the induction of gastric carcinoma in Wistar rats treated with N-methyl-N′-nitro-N-nitrosoguanidine (MNNG) were studied. Of 28 rats that were given drinking water containing 50 μg/ml MNNG for 25 wk, 21 developed gastric cancer after a further 25 wk. Of 12 rats similarly treated with MNNG and then given sc injections of 150 μg of tetragastrin (2x/day for weeks 26-29; 1x/wk for weeks 30-49), only 2 developed gastric tumors by week 50. It is suggested that the decrease in tumor development is related to the increased gastric secretion of acid brought about by the administration of gastrin. Gastrin did not influence the histological appearance of the few gastric adenocarcinomas that did develop. (21 refs.)

77-3753 **Transformation of Tracheal Epithelium Exposed In Vitro to N-Methyl-N′-Nitro-N-Nitrosoguanidine (MNNG) (Meeting Abstract).** (Eng.) Steele, V. S. (Cancer and Toxicology Program, ORNL, Oak Ridge, TN 37830) Marchok, A. C.; Nettesheim, P. *Proc Am Assoc Cancer Res* 18: 74; 1977. (no refs.)

77-3754 **Relation Between DNA Replication and Chemical Carcinogenesis in Mammalian Cell Cultures (Meeting Abstract).** (Eng.) Mironescu, S. (Bethesda, MD) *Proc Am Assoc Cancer Res* 18: 17; 1977. (no refs.)

77-3755 **Endogenous Formation of Carcinogenic N-Nitroso Compounds after Application of Drugs and Nitrite.** (Ger.) Schneider, J. (Pathologisches Institut der Medizinischen Akademie Erfurt, DDR-50 Erfurt, Nordhauser Strasse 74, E. Germany) Warzok, R.; Schwarz, H. *Exp Pathol (Jena)* 13(1): 32-43; 1977.

The endogenous nitrosation of piperazine, propylhexadrine, and ephedrine was investigated in long-term experiments with hooded and Wistar rats. One group of 15 rats received piperazine (80 mg/kg) and $NaNO_2$ (50 mg/kg) by gastric intubation twice a month for 7 mo. After a latent period of 254-432 days, 5/14 surviving rats developed malignant tumors of the nasal cavities (1), esophagus (1), leukoses (2), or soft tissue sarcoma (1). The tumor spectrum indicated the endogenous formation of N-nitrosopiperazines. Of 18 rats treated with propylhexadrine (40 mg/kg) and $NaNO_2$ for 6 mo, 10 developed tumors (4 paracecal reticulum cell sarcomas and 3 leukoses). Malignant tumors (mainly reticulum cell sarcomas and leukoses) also developed in 3/14 rats given ephedrine (80 mg/kg) and $NaNO_2$ (50 mg/kg) for 6 mo and in 13/30 rats fed a diet containing ephedrine (0.5%) and $NaNO_2$ (0.2%) for 50 days. No transplacental carcinogenic effect of piperazine and nitrite was demonstrated in hooded or Wistar rats, and there was no significant increase in tumor frequency in the offspring of pregnant rats treated with propylhexadrine and nitrite. The prevention of digestive tract neoplasms induced by nitrosable drugs is discussed. (39 refs.)

77-3756 **A New Carcinogen: N^6(Methylnitroso)adenosine (Meeting Abstract).** (Eng.) Anderson, L. M. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021) Giner-Sorolla, A.; Greenbaum, J.; Good, R. A. *Proc Am Assoc Cancer Res* 18: 79; 1977. (1 ref.)

77-3757 **In Vivo Autoradiography with ^{14}C-Labeled Nitrosoheptamethyleneimine in European Ham-**

sters (Meeting Abstract). (Eng.) Reznik-Schuller, H. (Abteilung fur Experimentelle Pathologie, Medizinische Hochschule, Hannover, Germany) Lijinsky, W.; Mohr, U. *Proc Am Assoc Cancer Res* 18: 27; 1977. (no refs.)

77-3758 **Angio-Immunoblastic Lymphadenopathy (AIL) and Immunoblastic Sarcoma of B Cells of the Armenian Hamster (Meeting Abstract).** (Eng.) Yerganian, G. (Sidney Farber Cancer Inst., Boston, MA 02115) Paika, I.; Gagnon, H.; Murthy, A. S. *Proc Am Assoc Cancer Res* 18: 205; 1977. (no refs.)

77-3759 **Three Antigens of Nitrosourea-Induced (NU) Rat Schwannomas (Meeting Abstract).** (Eng.) Harwood, S. E. (Dept. Pathology, Duke Univ. Medical Center, Durham, NC 27710) Bigner, D. D.; Day, E. D. *Proc Am Assoc Cancer Res* 18: 90; 1977. (no refs.)

77-3760 **Tumor Induction by Different Endogenously Formed N-Nitrosoureas in Hooded Rats.** (Ger.) Schneider, J. (Institut fur Allgemeine Pathologie und Pathologische Anatomie, Medizinische Akademie, Nordhauser Strasse 74, DDR-50 Erfurt, E. Germany) Warzok, R.; Osske, G.; Lehnguth, C. *Zentralbl Allg Pathol* 121(1/2): 61-75; 1977.

Methyl-, ethyl-, n-propyl-, isopropyl-, and n-butylurea (0.2%-0.5%) were given with sodium nitrite (0.2%-0.5%) to hooded rats to demonstrate the endogenous formation of carcinogenic nitrosamines and ensuing tumor formation. The experimental design was varied in eight experiments with respect to concentration, transplacental (starting on days 15 or 21 of pregnancy) or postnatal (birth to approx 50 days) application, and administration via food or drinking water or by gastric intubation. The transplacental action of endogenously formed ethylnitrosourea led to neurogenic neoplasms of the brain and trigeminal nerve in the offspring. Tumor incidence was especially high after the administration of 0.5% ethylurea and 0.5% $NaNO_2$ in the food from day 15 of pregnancy: 25/27 offspring developed tumors. In postnatal experiments with methylurea and $NaNO_2$ po or with isopropylurea and $NaNo_2$ by gastric intubation, neurogenic tumors and reticulum cell sarcomas of the paracecal region predominated. A single dose of 120 mg/kg isopropylurea and 60 mg/kg $NaNO_2$ in the drinking water on day 21 of pregnancy resulted in only a slight carcinogenic effect: 1 oligodendroglioma, 1 malignant neurilemmoma, 3 leukemias, and 1 plasmacytosis in a group of 16 rats. Administration of n-propylurea + $NaNO_2$ and n-butylurea + $NaNO_2$ led mainly to reticulum cell sarcomas of the paracecal region in 10/22 and 8/22 animals, respectively. In all experiments, control rats receiving urea compounds or $NaNO_2$ alone had a much lower tumor incidence. (58 refs.)

77-3761 **Transplacental Tumor Induction by N-Ethyl-N-nitrosourea in Different Species.** (Ger.) Warzok, R. (Institut fur Allgemeine Pathologie und Pathologische Anatomie, Medizinische Akademie, Nordhauser Strasse 74, DDR-50 Erfurt, E. Germany) Schneider, J.; Thust, R.; Scholtze, P.; Potzsch, H. D. *Zentralbl Allg Pathol* 121(1/2): 54-60; 1977.

Tumors were produced in several animal species by transplacental administration of N-ethyl-N-nitrosourea (ENU). ENU was given iv or ip to pregnant animals in the following doses: rats, rabbits, Dzungarian dwarf hamsters, and guinea pigs 40 mg/kg; Syrian golden hamsters 80 mg/kg; dogs 30 mg/kg; and rhesus monkeys 15-70 mg/kg. Tumor incidence in the offspring was: rats 51/51, rabbits 8/10, Syrian golden hamsters 9/20, Dzungarian dwarf hamsters 0/30, dogs 2/2, and rhesus monkeys 0/9 (6 yr survival). The most frequent tumors were CNS tumors in rats (51/51), renal tumors in rabbits (8/8), and thyroid tumors (5/9) in Syrian golden hamsters. Due to infection, results could not be obtained for the guinea pigs. As with other nitrosamines, the organ specificity of ENU tumor formation was species-specific. The results are compared to those of other researchers. (58 refs.)

77-3762 **Alkylation of DNA of Target Tissues of Mice at Doses of Alkylating Agents Which Induce Low Yields of Thymic Lymphomas (Meeting Abstract).** (Eng.) Frei, J. V. (Chester Beatty Res. Inst., Pollards Wood Res. Station, Chalfont St. Giles, Bucks, U.K.) Lawley, P. D. *Proc Am Assoc Cancer Res* 18: 26; 1977. (no refs.)

77-3763 **Retinyl Acetate Inhibits Mammary Carcinogenesis Induced by N-Methyl-N-nitrosourea.** (Eng.) Moon, R. C. (IIT Res. Inst., Chicago, IL 60616) Grubbs, C. J.; Sporn, M. B.; Goodman, D. G. *Nature* 267(5612): 620-621; 1977.

The effects of retinyl acetate on mammary carcinogenesis induced by N-methyl-N-nitrosourea (NMU) in female Sprague-Dawley rats were investigated. Rats were given two iv injections of NMU at doses of 5.0, 2.5, or 1.25 mg/100 g body wt 7 days apart. Three days after the second injection, the rats were placed on diets containing retinyl acetate (250 mg/kg diet) or placebo. Animals given the high dose of NMU and fed the placebo diet had a mammary cancer incidence of 83%, but animals treated with this dose and fed retinyl acetate had an incidence of 50%. A similar reduction was found in rats receiving the intermediate dose of NMU. No mammary cancer developed in rats receiving the low dose of NMU and retinyl acetate. Animals receiving this dose and placebo had a 20% incidence of mammary cancer. Retinyl acetate also caused a marked reduction in the total number of cancers and benign tumors, and it prolonged the latency period of mammary cancer at all three doses of NMU. These results demonstrate the efficacy of retinyl acetate in preventing experimental mammary cancer. (11 refs.)

77-3764 **Effect of Leupeptin on Induction of Lymphoblastic Leukemia in Mice by N-Nitrosobutylurea.** (Eng.) Kakizoe, T. (Dept. Urology, Faculty Medicine, Univ. Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 113, Japan) Sano, T.; Kawachi, T.; Sugimura, T.; Takeuchi, T.; Umezawa, H. *Gann* 68(3): 281-285; 1977.

An investigation was made of the effect of leupeptin on the induction of lymphoblastic leukemia in ICR/JCL female mice by N-nitrosobutylurea (NBU). NBU was administered as a 0.02% solution in drinking water for 10 wk; a 0.1% concentration of leupeptin was given in the diet. Group A was fed the leupeptin diet from the beginning, Group B received it after the end of NBU treatment, and Group C was fed a leupeptin-free control diet throughout. The av time of appearance of leukemia in groups A, B, and C was 115 ±50, 112 ± 43, and 100 ± 17 days, respectively. The differences between Groups A and B and Group C were significant, suggesting that leupeptin retarded leukemogenesis. However, leupeptin had no effect on the incidence and type of leukemia. (22 refs.)

77-3765 **Stimulation of Guanylate Cyclase By Chemical Carcinogens (Meeting Abstract).** (Eng.) Criss, W. E. (Howard Univ. Cancer Center and Dept. Biochemistry, Howard Univ. Medical Sch., Washington, DC 20060) Pradhan, T. K. *Proc Am Assoc Cancer Res* 18: 3; 1977. (no refs.)

77-3766 **Relative Carcinogenicity of Aliphatic Nitrosamines at Equimolar Doses (Meeting Abstract).** (Eng.) Lijinsky, W. (Frederick Cancer Res. Center, Frederick, MD 21701) *Proc Am Assoc Cancer Res* 18: 14; 1977. (no refs.)

77-3767 **Nitrosamine Formation in Cured Meat Products.** (Ger.) Kotter, L. (Institut fur Hygiene und Technologie der Lebensmittel tierischen Ursprungs der Universitat Munchen-Fachbereich Tiermedizin, Munich, W. Germany) Schmidt, H.; Fischer, A. *Arch Lebensmittelhyg* 28(1): 8-11; 1977.

The effect of various additives (sodium ascorbate, ascorbic acid, dextrose, glucono-δ-lactone) on nitrosamine formation in raw sausages was investigated. To provoke reactions, 10 mg/kg diethylamine was added to some of the batches. After different maturation times, the sausages were examined for dimethylnitrosamine, diethylnitrosamine, nitrosopiperidine, nitrosopyrrolidine, methylethylnitrosamine, and nitrosomorpholine by gas chromatography/mass spectrometry. No nitrosamines were detected in the sausages without added diethylamine (detection limit 1 nanogram). In some of the samples to which diethylamine was added, traces of diethylnitrosamine (at most, 3.5 μg/kg) were present. The additives showed no effects. Three ways of restricting possible nitrosamine formation in foods or in the human stomach are discussed: ensuring that the diet is low in nitrosating substances; ensuring that foods are low in amines and that the use of drugs containing amines is controlled; avoiding handling methods that favor reactions between nitrosating substances and nitrosatable amines in foods. (35 refs.)

77-3768 **Carcinogenic Effect of N-Nitroso Compounds on Bivalve Mussels *Unio pictorum*.** (Rus.) Khudolei, V. V. (Res. Inst. Oncology, Acad. Medical Sciences, USSR) Sirenko, O. A. *Biull Eksp Biol Med* 83(5): 571-579; 1977.

When dissolved in the tank water in doses of 200-400 ppm, diethyl- and dimethylnitrosamines, respectively, induced digestive tract neoplasms (basophilic cell tumors) in 16/95 and 6/17 mussels that survived to the time of appearance of the first tumor (38-39 days). The respective compounds also induced lymphatic leukemia in 7 and 1 mussels, chiefly in combination with tumors of the digestive tract. Methylnitrosoguanidine induced only inflammatory changes at the injection site. Mollusks are concluded to be a useful biological indicator of hydrosphere pollution by chemical carcinogens. (11 refs.)

77-3769 **Cytoplasmic Abnormalities Induced in Rat Liver Cells By Diethylnitrosamine (Meeting Abstract).** (Eng.) Higgins, P. J. (Memorial Sloan-Kettering Cancer Center, NY 10021) Bendich, A. *Proc Am Assoc Cancer Res* 18: 29; 1977. (no refs.)

77-3770 **Adrenergic Component in the Hepatotropic Carcinogenic Effect of Diethylnitrosamine.** (Eng.) Gurkalo, V. K. (N. N. Petrov Res. Inst. Oncology, Ministry Public Health USSR, Leningrad, USSR) Zabezhinskii, M. A.; Pliss, G. V.; Krylov, S. S. *Biull Eksp Biol Med* 83(4): 455-458; 1977.

The effect of epinephrine and its antagonist pyroxan on diethylnitrosoamine (DENA)-induced carcinogenesis was studied in 30 random-bred albino male rats. The animals were subdivided into three groups: Group 1 (controls) was treated with DENA (100 mg/liter drinking water for 4 mo, po) alone, Group 2 received DENA + epinephrine (2.5 μg/kg 3x/wk for 6 mo, sc), and Group 3 received DENA + pyroxan (25 mg/kg 3x/wk for 6 mo, sc). Six months later, all animals in Groups 2 (9/9) and 3 (8/8) and 3/7 animals in Group 1 developed hyperplastic nodules in the liver. Groups 1 and 2 animals developed multiple 0.6- to 1.0-cm nodes, but Group 3 animals developed significantly smaller (0.100.2 cm) nodes. Hepatocellular carcinoma developed in the hyperplastic nodules of 2/3 Group 1 rats, 6/9 Group 2 rats, but in only 2/8 Group 3 rats. (10 refs.)

77-3771 **Transplacental Carcinogenic Action of Diethylnitrosamine in the Dzungarian Hamster.** (Ger.) Thust, R. (Institut fur Allgemeine Pathologie und Pathologische Anatomie, Medizinische Akademie, Nordhauser Strasse 74, DDR-50 Erfurt, E. Germany) Warzok, R. *Zentralbl Allg Pathol* 121(1/2): 82-86; 1977.

Tumors were produced in the offspring of Dzungarian hamsters treated with diethylnitrosamine (DEN) during gestation. DEN was given ip under ether anesthesia in a single dose (30 mg/kg in saline) to 15 pregnant Dzungarian hamsters at 3 days to 6 hr before delivery. The offspring were weaned at 4 wk. Of the 29 hamsters, 21 survived until the appearance of the first tumors. Tumors appeared from 127-570 days. Lung tumors appeared in 76.2% of the animals, most of which were benign. Five of the lung tumors were papillary or tubular carcinomas. Five animals with lung tumors also had additional tumors--an adenoma of the thyroid, mammary gland, and liver and a well-differentiated prostatic carcinoma. One animal had an ovarian cyst and a malignant lymphoma. In 46 controls that survived 200 days, two ovarian cyst, one squamous cell carcinoma of the mouth, and one papilloma of a bronchus were found. The organ specificity of DEN is different in different species, even in different breeds of one species. The tumor spectrum is usually the same after transplacental or postnatal application. (14 refs.)

77-3772 **Mammalian mRNA Transplantation of the Liver Ribosome Subunits Isolated from Dimethylnitrosamine-treated Mice (Letter to Editor).** (Eng.) Delpino, A. (Regina Elena Inst. Cancer Res., Rome, Italy) Ferrini, U. *Eur J Cancer* 13(7): 773-774; 1977.

The translation efficiency of purified liver ribosome subunits, isolated from dimethylnitrosamine (DMN)-treated rats, was tested in an in vitro system programmed with rabbit globin messenger RNA (mRNA) and supplemented with heterologous initiation factors. Mice received 50 mg/kg body wt DMN ip 3 hr before killing. Liver ribosome subunits were isolated by high salt gradient centrifugation directly from detergent-treated postmitochondrial supernatants. The subunits isolated from DMN-treated mice were able to translate on mammalian mRNA with the same efficiency as control subunits in the presence of both fixed and variable amounts of initiation factors. These results led to the assumption that within the first 3 hr after DMN injection, the protein-synthesizing capacity of the subunits derived from DMN-generated monomers is unchanged. Therefore, the ribosomes per se do not play a significant role in the inhibition of protein synthesis following a toxic dose of DMN. (8 refs.)

77-3773 **Analysis By Benzoylated-DEAE-Cellulose of Carcinogen-Induced DNA Damage In Vivo (Meeting Abstract).** (Eng.) Stewart, B. W. (Sch. Pathology, Univ. New South Wales, Kensington, N.S.W. 2033 Australia) Huang, P. H. *Proc Am Assoc Cancer Res* 18: 23; 1977. (no refs.)

77-3774 **Protein Bound Carboxyl-Methyl Ester as a Precursor of Methanol Formation During Oxidation of Dimethylnitrosamine In Vitro (Meeting Abstract).** (Eng.) Kim, S. (Fels Res. Inst. and Dept. Pathology, Temple Univ. Sch. Medicine, Philadelphia, PA 19140) Lotlikar, P. D.; Chin, W.; Magee, P. *Proc Am Assoc Cancer Res* 18: 48; 1977. (no refs.)

77-3775 **Screening for Nitrosodimethylamine in Human Urine and Experiments on the Formation of This Carcinogen from the Analgesic Amidopyrine in Bacterial Model Systems.** (Eng.) Sander, J.; Walz, G. *In: Environmental N-Nitroso Compounds: Analysis and Formation. Proceedings of a Working Conference held at the Polytechnical Institute, Tallinn, Estonian SSR, 1-3 October 1975.* Walker, E. A.; Bogovski, P.; Griciute, L.; Davis, W., eds. International Agency for Research on Cancer. (Lyon, France) IARC Scientific Publication No. 14, pp. 291-300; 1977.

The analgesic amidopyrine (AP), which has been banned in the US but is generally available in West Germany and other countries, readily forms the highly carcinogenic compound dimethylnitrosamine (DMNA) when reacted with nitrite in vitro. To investigate whether the easy formation of DMNA from AP and nitrite might represent a significant health risk in humans, tests for DMNA in the urine of patients were performed. In other experiments, conditions for the in vitro formation of DMNA from AP were analyzed in a model system. Upon analysis of selected urine specimens, 7 developed color equivalent to a concentration of 2-4 μg/ml DMNA and 3 developed color stronger than that produced by 8 μg/ml DMNA. Synthesis of DMNA from AP in medium in which *Escherichia coli* was responsible for the reduction of nitrate to nitrite resulted in max yields in the pH range 4.5-5: 2.5 mg DMNA were formed from 250 mg AP in 16 hr at pH 5 with a concentration of nitrate of 1 g/kg. Ascorbic acid was an effective inhibitor of DMNA formation. (21 refs.)

77-3776 **Induction of Esophageal Carcinoma with *N*-Methyl-*N*-Benzyl Nitrosamine (MBZN) in the Rat (Meeting Abstract).** (Eng.) Stinson, S. F. (Lung Cancer Branch, NCI, Bethesda, MD, 20014) Smith, J. M.; Sporn, M. B. *Proc Am Assoc Cancer Res* 18: 38; 1977. (1 ref.)

77-3777 **Vascular Changes in Neoplasia and Hyperplasia of the Urinary Bladder (Meeting Abstract).** (Eng.) Ito, N. (1st Dept. Pathology, Nagoya City Univ. Medical Sch., Nagoya, Japan) Tatematsu, M.; Shirai, T.; Cohen, S. M.; Arai, H.; Fukushima, S. *Proc Am Assoc Cancer Res* 18: 39; 1977. (no refs.)

77-3778 **Metabolism of the Pancreatic Carcinogen *N*-Nitrosobis(2-Oxopropyl)amine After Oral and Ip Administration to Hamsters (Meeting Abstract).** (Eng.) Gingell, R. (Eppley Inst. Res. Cancer, Omaha, NB 68105) Pour, P.; Langenbach, R. *Proc Am Assoc Cancer Res* 18: 39; 1977. (no refs.)

77-3779 **Investigations of the Reaction Kinetics in the Formation of 7-Chloro-2N-nitrosomethylamino-5-phenyl-3H-1,4,-benzodiazepine-4-oxide.** (Ger.) Kinawi, A. (Freie Universitat Berlin, Zentralinstitut fur Biochemie und Biophysik, Ostpreussendamm 111, 1000 Berlin 65, W. Germany) Doring, D.; Witte, I. *Arzneim Forsch* 27(4): 747-750; 1977.

The influence of alcohol, ascorbic acid, phenol, and thiocyanic acid on the formation of 7-chloro-2N-nitrosomethylamino-5-phenyl-3H-1,4-benzodiazepine-4-oxide (N-nitrosochlordiazepoxide) from chlordiazepoxide and nitrous acid was investigated by high-performance liquid chromatography. (23 refs.)

77-3780 **Acute Leukemia Following Alkylating Agent Therapy of Ovarian Cancer (Meeting Abstract).** (Eng.) Reimer, R. R. (Environmental Epidemology and Medicine Branches, NCI, Bethesda, MD 20014) Hoover, R.; Fraumeni, J. F.; Young, R. C. *Proc Am Assoc Cancer Res* 18: 331; 1977. (no refs.)

77-3781 **Factors Affecting O^6-Methylguanine Levels in Rat Liver DNA After Treatment with Dimethylnitrosamine and 1,2-Dimethylhydrazine (Meeting Abstract).** (Eng.) Pegg, A. E. (Dept. Physiology and Specialized Cancer Center, Pennsylvania State Univ., Coll. Medicine, Hershey, PA 17033) Hui, G.; Rogers, K. J. *Proc Am Assoc Cancer Res* 18: 13; 1977. (no refs.)

77-3782 **Small-Bowel Resection Enhances Colonic Carcinogenesis by Dimethylhydrazine (DMH) and Azoxymethane (AOM) (Meeting Abstract).** (Eng.) Oscarson, J. E. (Surgical Services, Massachusetts General Hosp., and Dept. Surgery, Harvard Medical Sch., Boston, MA 02114) Williamson, R. C.; Veen, H. F.; Bauer, F. L.; Malt, R. A. *Proc Am Assoc Cancer Res* 18: 43; 1977. (no refs.)

77-3783 **The Influence of Adrenoreceptor Activity on Cell Proliferation in Colonic Crypt Epithelium and in Colonic Adenocarcinomata.** (Eng.) Tutton, P. J. (Dept. Anatomy, Monash Univ., Clayton, Victoria, 3168, Australia) Barkla, D. H. *Virchows Arch (Cell Pathol)* 24(2): 139-146; 1977.

The effects of chemical sympathectomy and of the injection of amines or amine-receptor blocking drugs on cell proliferation in colonic crypts and in dimethylhydrazine-induced colonic carcinomas in male Sprague-Dawley rats were examined by a stathmokinetic technique. The rats had received weekly sc injections of 21 mg/kg DMH for 21 wk. In animals chemically sympathectomized by iv injection of 6-hydroxydopamine (100 mg/kg), cell proliferation essentially ceased in the colonic crypts but continued at a normal rate in the tumors. Stimulation of α-adrenoceptors by metaraminol, a drug with properties similar to noradrenaline, accelerated cell proliferation in the colonic crypts but not in the tumors. Conversely, blockade of α-adrenoceptors by phentolamine (10 mg/kg) inhibited cell proliferation in the crypts but not in the tumors. Injection of adrenaline, predominantly a β-adrenergic agonist, inhibited cell proliferation in the tumors but not in the colonic crypts, but blockage of β-adrenoceptors by propranolol (20 mg/kg) accelerated cell proliferation in the tumor but not in the crypts. It is postulated that cell proliferation in the crypts of Lieberkuhn in the rat colon resembles that in the jejunum in being controlled by the autonomic nervous system. However, tumor cell proliferation does not appear to be subject to such regulation. (27 refs.)

77-3784 **Tumorigenicity of the N′-Acetyl Derivative of 4-Hydroxymethylphenylhydrazine, An Ingredient of *Agaricus Bisporus* (Meeting Abstract).** (Eng.) Toth, B. (Eppley Inst., Univ. Nebraska Medical Center, Omaha, NB 68105) Nagel, D. *Proc Am Assoc Cancer Res* 18: 15; 1977. (no refs.)

77-3785 **The Primary Effect of Carcinogens on the Lactate Dehydrogenase Isoenzyme Pattern in the Rat Kidney.** (Rus.) Bozhekov, V. M. (Lab. Tumor Cell Genetics, Inst. Cytology, Acad. Sciences USSR, Leningrad, USSR) Khodosova, I. A.; Medvedeva, N. D. *Tsitologiia* 19(4): 410-416; 1977.

The effect of a single ip injection of dimethylnitrosamine (DMNA: 30 μg/g) and 4-dimethylaminoazobenzene (DAB: 250 μg/g) on kidney lactate dehydrogenase (LDH) activity was studied in random-bred albino rats. The animals were sacrified on days 1-53 after injection, and the LDH pattern in the kidney tissue was assessed electrophoretically. Both carcinogens increased the LDH-5 content (no further details). This finding may not be associated with the carcinogenic effect of DMNA and DAB, but may reflect a nonspecific cellular reaction. (13 refs.)

77-3786 **Primary Effect of Dimethylaminoazobenzene on Transcription of Unique Rat Liver DNA Sequences.** (Rus.) Barskaia, T. V. (Lab. Tumor Cell Genetics, Inst. Cytology, Acad. Sciences USSR, Leningrad, USSR) Zakharova, N. V.; Olenov, Iu. M. *Tsitologiia* 19(4): 454-457; 1977.

Random-bred albino rats were inoculated with 4-dimethylaminoazobenzene (DAB: 25 mg/100 g, ip); 24 hr later, the animals were sacrificed and liver RNA was isolated. In a competitive hybridization experiment with unique-sequence DNA, it was found that nuclear RNA from DAB-treated rats showed less hybridization with DNA than the RNA from untreated animals. In an RNA-RNA hybridization experiment, the RNA from DAB-treated rats showed a greater capacity to bind the probe than the RNA from untreated animals. These results suggest that DAB blocked specific regions of the unique-sequence DNA and intensified transcription from other regions. (10 refs.)

77-3787 **The Decreased Degradation of Nuclear Nonhistone Proteins in Hepatocarcinogenesis (Meeting Abstract).** (Eng.) Fiala, S. (VAC, Martinsburg, WV 25401) Kettering, W.; Ostrander, H. *Proc Am Assoc Cancer Res* 18: 43; 1977. (43 refs.)

77-3788 **Use of Terbium Fluorescence Enhancement to Detect Modified 5′GMP Moieties in Ribosomal RNA from 3′ MeDAB-Fed Rat Livers (Meeting Abstract).** (Eng.) Ringer, D. (Noble Foundation, Inc., Ardmore, OK 73401) Burchett, S.; Kizer, D. E. *Proc Am Assoc Cancer Res* 18: 178; 1977. (no refs.)

77-3789 **Distribution of Antigenic Markers of Differentiation--Ligandin and α-Fetoprotein--at Early Stages of Chemical Carcinogenesis in the Rat Liver.** (Rus.) Bannikov, G. A. (Oncological Scientific Center, Acad. Medical Sciences USSR, Moscow, USSR) Gel'shtein, V. I.; Chipysheva, T. A. *Vestn Akad Med Nauk SSSR* (3): 39-41; 1977.

Histochemical changes in the liver cell populations at early stages of chemical carcinogenesis were studied in random-bred albino rats fed a diet containing 3′-methyl-4-dimethylaminoazobenzene (3′-MeDAB) and 2-acetylaminofluorene (2-AAF). Animals were exposed to the carcinogens for 7-30 days and then sacrificed, and localization ofα-fetoprotein and ligandin in tumor tissue was assessed by immunofluorescence tests. α-Fetoprotein could not be detected in control animals, and ligandin had a characteristic localization in the highly differentiated centrilobular regions of the liver. However, rats exposed to 3′-MeDAB and 2-AAF for 3-4 wk showed a proliferation of oval cells, basophilic hepatocytelike cells, cubical epithelium of the bile ducts, oxyphilic epithelium, and hyperplastic nodules. The content of ligandin was elevated in the nodules and in the oxyphilic columnar epithelium; α-fetoprotein could be detected only in the basophilic hepatocytelike cells in the zones of oval cell proliferation. (10 refs.)

77-3790 **Organ Specificity of Carcinogen Induced Changes in tRNA Methylases (Meeting Abstract).** (Eng.) Wainfan, E. (Lindsley F. Kimball Res. Inst New York Blood Center and Memorial Sloan-Kettering Cancer Center, New York, NY 10021) Randle, S. S.; Balis, M E. *Proc Am Assoc Cancer Res* 18: 10; 1977. (no refs.)

77-3791 **Alterations in Template Activity of the Nuclear DNA of Different Cell Populations in Precancerous Liver (Meeting Abstract).** (Eng.) Goodman, J. I

(Dept. Pharmacology, Michigan State Univ., East Lansing, MI 48824) Adams, M. P. *Proc Am Assoc Cancer Res* 18: 16; 1977. (no refs.)

77-3792 **Studies on Peroxisomal Proliferation in Preneoplastic Livers of Rats Fed 2-AAF and of Mice Fed α-BHC (Meeting Abstract).** (Eng.) Tsukada, H. (Cancer Res. Inst., Sapporo Medical Coll., Sapparo, Japan) Gotoh, M.; Mochizuki, Y.; Furukawa, K. *Proc Am Assoc Cancer Res* 18: 38; 1977. (2 refs.)

77-3793 **Sequential Alkaline Phosphatase Changes in Hyperplastic and Neoplastic Urothelium of Mice Induced by 2-Acetylaminofluorene (Meeting Abstract).** (Eng.) Highman, B. (Univ. Arkansas Coll. Medicine, Little Rock, AR) Frith, C. H.; Littlefield, N. A. *Toxicol Appl Pharmacol* 41(1): 155-156; 1977. (no refs.)

77-3794 **Studies on Induction and Inhibition of N-Hydroxylation of N-2-Fluorenylacetamide (2-FAA) in Rat Liver (Meeting Abstract).** (Eng.) Malejka-Giganti, D. (VA Hosp. and Dept. Lab. Medicine and Pathology, Univ. Minnesota, Minneapolis, MN 55417) McIver, R. *Proc Am Assoc Cancer Res* 18: 32; 1977. (no refs.)

77-3795 **Lack of Carcinogenic Effect after Application of Amines and Amides Together with Nitrite in Rabbits.** (Ger.) Schneider, J. (Pathologisches Institut der Medizinischen Akademic Erfurt, DDR-50 Erfurt, Nordhauser Strasse 74, E. Germany) Warzok, R.; Osske, G.; Potzsch, H. D. *Exp Pathol (Jena)* 13(1): 78-80; 1977.

Young rabbits of both sexes were treated with nitrosable compounds and sodium nitrite as follows: 13 animals received 0.1% methylurea in food and 0.1% $NaNO_2$ in drinking water for 100 days, 20 animals received 0.2% dimethylbenzylamine in drinking water and 0.15% $NaNO_2$ in the diet for 100 days, and 20 animals were fed 0.2% diethylaminohydrochloride and 0.2% $NaNO_2$ for 63 days. No carcinogenic effect of the amines and amides was demonstrated at the concentrations used. (12 refs.)

77-3796 **Microsomal N-Hydroxylation of *trans*-$4'$-Halo-4-acetamidostilbenes.** (Eng.) Gammans, R. E. (Dept. Pharmacology, Univ. Minnesota, Minneapolis, MN 55455) Sehon, R. D.; Anders, M. W.; Hanna, P. E. *Drug Metab Dispos* 5(3): 310-316; 1977.

Hamster liver microsomes catalyzed the N-hydroxylation of *trans*-4-acetamidostilbene and its $4'$-Cl and $4'$-F analogs. The $4'$-OH derivative of *trans*-4-acetamidostilbene and the glycolamides of the $4'$-Cl and $4'$-F compounds were also detected and quantitated. The kinetics of metabolism of the acetamidostilbenes were determined. While the apparent Km values of N-hydroxylation of the four substrates were similar, the maximal velocities (V max) showed marked variations. The Vmax for the $4'$-Br analog was 16% of that of *trans*-4-acetamidostilbene; the rate of N-hydroxylation of the $4'$-Cl and $4'$-F analogs was only 3% of that of the parent compound. The results indicated that the rate of microsomal N-hydroxylation is markedly influenced by relatively small changes in the structural and physicochemical properties of N-arylacetamides. Since this N-hydroxylation is an obligatory step in arylamide-mediated carcinogenesis, further studies of the modification of this process are indicated, perhaps allowing for a detoxification pathway. (31 refs.)

77-3797 **Reactivity of the Carcinogen N-Hydroxy-1-Naphthylamine with Nucleic Acids (Meeting Abstract).** (Eng.) Kadlubar, F. F. (Natl. Center for Toxicology Res., Jefferson, AR 72079) Miller, J. A.; Miller, E. C. *Proc Am Assoc Cancer Res* 18: 30; 1977. (no refs.)

77-3798 **The Glucuronic Acid Conjugate of 4-Aminobiphenyl In Dog Urine (Meeting Abstract).** (Eng.) Radamski, J. L. (Univ. Miami, Miami, FL 33152) Moreno, H. R.; Hearn, W. L. *Proc Am Assoc Cancer Res* 18: 66; 1977. (1 ref.)

77-3799 **Studies on Nucleolar U3 RNA (Meeting Abstract).** (Eng.) Ro-Choi, T. (Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX 77030) Pike, L. M.; Henning, D. *Proc Am Assoc Cancer Res* 18: 173; 1977. (1 ref.)

77-3800 **Ligandin (Glutathione S-Transferase Brat) in Cell Culture Systems (Meeting Abstract).** (Eng.) Smith, G. J. (Fels Res. Inst., Temple Univ. Sch. Medicine, Philadelphia, PA 19140) Litwack, G. *Proc Am Assoc Cancer Res* 18: 40; 1977. (no refs.)

77-3801 **Change in the Paramagnetic Properties of Liver Tissue in Mice Exposed to Benzene Vapor.** (Rus.) Sergeev, A. I. (Inst. Chemical Physics, Acad. Sciences USSR, Moscow, USSR) Naidich, V. I.; Bunto, T. V. *Dokl Akad Nauk SSSR* 234(2): 472-474; 1977.

The toxic effect of benzene vapor was studied in CBA mice. Animals were exposed to 22 or 35 mg/liter of benzene for 3-5.5 hr and sacrificed, and the content of free radicals and cytochrome p-450 in the liver tissue was assessed by electron paramagnetic resonance. Exposure to benzene vapor caused a temporal elevation of free-radical and cytochrome P-450 concentrations. Max values of free radicals were observed on days 4.4-5 after a 3-hr exposure and on days 2-3 after a 5.5-hr exposure to 22 mg/liter benzene. With 35 mg/liter benzene, this response was accelerated: a max concentration of free radicals was observed on day 1 after a 5.5-hr exposure. The kinetics were similar for cytochrome P-450. (11 refs.)

77-3802 **Azaserine-Induced Nodules and DNA Damage in Pancreas of Several Species (Meeting Abstract).** (Eng.) Roebuck, B. D. (Dartmouth Medical Sch., Hanover, NH 03755) Lilja, H. S.; Longnecker, D. S. *Proc Am Assoc Cancer Res* 18: 67; 1977. (no refs.)

77-3803 **Patterns of Invasive Carcinoma of Rat Urinary Bladders Induced by Lifetime Feeding of N-[4-(5-Nitro-2-Furyl)-2-Thiazolyl]formamide (FANFT) (Meeting Abstract).** (Eng.) Arai, M. (Dept. Pathology, St. Vincent Hosp., Worcester, MA 01604) Jacobs, J. B.; Cohen, S. M.; Friedell, G. H. *Proc Am Assoc Cancer Res* 18: 192; 1977. (no refs.)

77-3804 **Binding of 2-Amino-4-(5-Nitro-2-Furyl)-2-^{14}C-Thiazole (ANFT) To Yeast Transfer RNA, Using Rat Liver Microsomes (Meeting Abstract).** (Eng.) Swaminathan, S. (Dept. Human Oncology, Univ. Wisconsin Medical Sch., Madison, WI 53706) Wong, R. C.; Lower, G. M.; Bryan, G. T. *Proc Am Assoc Cancer Res* 18: 187; 1977. (no refs.)

77-3805 **Repair In Vivo of Liver Deoxyribonucleic Acid Damaged by Hycanthone and Related Compounds.** (Eng.) Sarma, D. S. (Dept. Pathology, Univ. Toronto Medical Sch., Toronto, Ontario, Canada M5S 1A8) Zubroff, J.; Rajalakshmi, S. *Mol Pharmacol* 13(4): 719-725; 1977.

Liver DNA damage and its subsequent repair in vivo, induced by the antischistosomal drug hycanthone methanesulfonate (HyMS) and its analog, were studied by sedimenting DNA in alkaline and neutral sucrose gradients. Within 1 hr of ip administration to Wistar rats, HyMS (25 μg/g) caused liver DNA damage that could be monitored as slowly sedimenting DNA (compared with control) in alkaline as well as neutral sucrose gradients. By 24 hr, the hepatic DNA of rats given HyMS (100 μg/g) sedimented into the 2.3 M sucrose layer of the neutral sucrose gradients, suggesting repair of the DNA lesions. However, when the same DNA was sedimented in alkaline sucrose gradients, anomalies were observed up to 48 hr after drug administration. At the same dose, two analogs of Hy, the chloroindazole derivative and its N-oxide, which are less hepatotoxic, teratogenic, and mutagenic than Hy, failed to induce the DNA damage measurable as slowly sedimenting DNA in neutral sucrose gradients. Nonetheless, these two analogs, like Hy, intercalated into DNA. Niridazole (200 μg/g), another antischistosomal drug, neither intercalated into DNA nor induced hepatic DNA damage measurable as slowly sedimenting DNA in either neutral or alkaline sucrose gradients. (40 refs.)

77-3806 **Testing the Carcinogenicity of an Anti-Schistosomal Drug, Hycanthone, in Schistosoma Mansoni-Infected and Non-Infected Mice and Hamsters (Meeting Abstract).** (Eng.) Bulay, O. (Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, Omaha, NB 68105) Urman, H.; Patil, K.; Clayson, D. b.; Shubik, P. *Proc Am Assoc Cancer Res* 18: 39; 1977. (no refs.)

77-3807 **Microsome-Dependent Covalent Binding of the Carcinogen, Trichloroethylene, to Cellular Macromolecules (Meeting Abstract).** (Eng.) Banerjee, S. (Lab. Organic Chemistry and Carcinogenesis, Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY 10016) Van Duuren, B. L.; Goldschmidt, B. M. *Proc Am Assoc Cancer Res* 18: 34; 1977. (1 ref.)

77-3808 **Carcinogenic Potential of Chlorinated Ethylenes. Tentative Molecular Rules.** (Eng.) Henschler, D.; Bonse, G.; Greim, H. *In: Environmental Pollution and Carcinogenic Risks.* (Lyon: International Agency for Research on Cancer): IARC Scientific Publications No. 13, INSERM Symposia Series Vol. 52, pp. 171-175; 1976.

The mechanisms of bioactivation and the mutagenic activity of the chlorinated ethylenes were studied with a short-term in vitro system using metabolic activating liver microsomal enzymes. Chlorinated ethylenes were activated in mammalian metabolism to oxiranes. Asymmetric chlorine substitution of the ethylenes and oxiranes rendered the molecules unstable and mutagenic. Vinyl chloride was the most active; trichloroethylene and vinylidene chloride were far less active but still significantly so. Chlorinated ethylenes metabolized via symmetric oxiranes (tetrachloroethylene, cis- and trans-1.2-dichloroethylene) were relatively stable, and were not mutagenic. It was concluded that mutagenic activity and possible carcinogenic potential were related directly to oxirane stability. (13 refs.)

77-3809 **Pharmacokinetics of Vinyl Chloride in the Rat.** (Eng.) Bolt, H. M. (Inst. Toxicology, Univ. Tubingen, Tubingen, W. Germany) Laib, R. J.; Kappus, H.; Buchter, A. *Toxicology* 7(2): 179-188; 1977.

When rats were exposed to ^{14}C-vinyl chloride (VC) in a closed system, the VC in the atmosphere equilibrated with that in the animals tissues within 15 min. This course of equilibration was determined in male Wistar rats treated ip with 6-nitro-1,2,3,-benzothiadiazole at a dose (50 mg/kg) sufficient to block the metabolism of 200-1,200 ppm VC for 4 hr. Saturation of the VC-metabolizing enzymes occurred at an atmospheric VC concentration of 250 ppm. Pharmacokinetic analysis showed no significant accumulation of VC or its major metabolites following repeated administration of the compound. The results support the theory that a reactive, short-lived metabolite, which occurs only in low concentrations, may be responsible for the toxic effects of VC. (25 refs.)

77-3810 **Liver Angiosarcomas Occasioned by Exposition to Vinyl Chloride (Meeting Abstract).** (Eng.) Panh Meng, H. (Laboratoire d'Anatomie Pathologique, C.H.U., B.P. 217 X, 38043 Grenoble Cedex, France) Faure, H.; Pasquier, D.; Couderc, P. *Acta Pharmacol Toxicol [Suppl] (Kbh)* 41(2): 331; 1977. (no refs.)

77-3811 **Vinyl Carbamate, A Potent Carcinogen and A Possible Urethan Metabolite in the Mouse (Meeting Abstract).** (Eng.) Dahl, G. A. (McArdle Lab., Univ. Wisconsin, Madison, WI 53706) Miller, E. C.; Miller, J. A. *Proc Am Assoc Cancer Res* 18: 6; 1977. (4 refs.)

77-3812 **Enhancement of Urethan Tumorigenesis in Mouse Lung Following Multiple Injections of Butylated Hydroxytoluene (Meeting Abstract).** (Eng.) Witschi, H. P. (Dept. Pharmacologie, Faculte de Medecine, Univ. Montreal, Montreal, Canada) Lock, S. *Toxicol Appl Pharmacol* 41(1): 156; 1977. (no refs.)

77-3813 **Effect of Urethane on the T-Lymphocyte Count in the Spleens of Mice That Are Resistant and Susceptible to Cancer.** (Rus.) Porugova, G. M. (Inst. Genetics and Cytology, Acad. Sciences Belorussian SSR, USSR) *Dokl Akad Nauk SSSR* 21(4): 359-361; 1977.

The immunodepressive effect of a single injection of urethane (1 mg/g ip) was studied in Af (susceptible) and C3H/Sn and C57BL/10Sn (resistant) mice. The number of T lymphocytes in the spleen was assessed quantitatively by in vitro cytotoxicity tests. Urethane-treated mice showed a significant reduction in number of T cells. This decrease was most pronounced in Af mice (50%); C3H/Sn and C57BL/10Sn mice showed 33% and 20% reductions, respectively. The immunodepressive effect of urethane was positively correlated with its previously reported carcinogenic effect: Af, c3H/Sn, and C57BL/10Sn mice exposed to urethane developed 32, 2.5, and 0.09 lung adenomas, respectively, 5 mo later. (7 refs.)

77-3814 **Altered Regulation of Hepatic Heme Biosynthesis and Mixed Function Oxidase Activity in Ethionine-Fed Rats (Meeting Abstract).** (Eng.) Woods, J. S. (Natl. Inst. Environmental Health Sciences, NIH, Research Triangle Park, NC 27709) *Proc Am Assoc Cancer Res* 18: 8; 1977. (no refs.)

77-3815 **Elevation of Progesterone Levels in Immature Chicks By the Carcinogen Ethionine (Meeting Abstract).** (Eng.) Sharma, O. K. (Univ. Colorado Medical Center, Denver, CO 80262) Borek, E. *Proc Am Assoc Cancer Res* 18: 27; 1977. (1 ref.)

77-3816 **Evaluation of Effects of Four Hair Dye Components on Epstein-Barr Virus (EBV) and Herpesvirus Saimiri (HVS) Systems (Meeting Abstract).** (Eng.) Armstrong, G. R. (NCI, Bethesda, MD 20014) Easton, J. M. *Proc Am Assoc Cancer Res* 18: 20; 1977. (no refs.)

77-3817 **Metabolism of the Dyestuff Intermediate, 2,4-Diaminoanisole, in the Rat (Meeting Abstract).** (Eng.) Grantham, P. H. (NCI, Bethesda, MD 20014) Mohan, L. C.; Benjamin, T. T.; Roller, P. P. *Toxicol Appl Pharmacol* 41(1): 160; 1977. (no refs.)

77-3818 **A Carcinogenicity Study of the Pesticide Dieldrin in Hamsters (Meeting Abstract).** (Eng.) Cabral, J. R. (Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, Omaha, NB 68105) Shubik, P.; Bronczyk, S. A.; Hall, R. K. *Proc Am Assoc Cancer Res* 18: 28; 1977. (no refs.)

77-3819 **Tris(2,3-Dibromopropyl) Phosphate: Mutagenicity of a Widely Used Flame Retardant.** (Eng.) Prival, M. J. (Office Toxic Substances WH-557, Environmental Protection Agency, Washington, D.C. 20460) McCoy, E. C.; Gutter, B.; Rosenkranz, H. S. *Science* 195(4273): 76-78; 1977.

Studies with tris(2,3-dibromopropyl) phosphate indicated that it is mutagenic to strains of *Salmonella typhimurium* requiring histidine and that the mutagenic activity is retained in a treated fabric. The results suggested that some of the mutagen can be released from the fabric and absorbed through the skin. (15 refs.)

77-3820 **Inhibition of DNA Synthesis in BHK Fibroblasts Treated In Vitro with Potassium Dichromate.** (Eng.) Levis, A. G. (Inst. Animal Biology, Univ. Padova, Via Loredan 10, I-35100 Padova, Italy) Buttignol, M.; Vettorato, L. *Experientia* 33(1): 82-84; 1977.

The effects of potassium dichromate on BHK fibroblasts were investigated. Although the uptake of labeled thymidine into the intracellular pool was stimulated, DNA replication was inhibited; this inhibitory effect was due to the reduced trivalent chromium interacting with ligands on the DNA molecule. (18 refs.)

77-3821 **Metal Carcinogenesis: A Study of the Carcinogenic Activity of Solid Metal Alloys in Rats.** (Eng.) Gaechter, A. (Rush-Presbyterian-St. Luke's Medical Center, 1753 W. Congress Parkway, Chicago, IL 60612) Alroy, J.; Andersson, G. B.; Galante, J.; Rostoker, W.; Schajowicz, F. *J Bone Joint Surg [Am]* 59-A(5): 622-624; 1977.

The carcinogenicity of seven metallic alloys used as surgical implants in humans was studied. Solid rods of each alloy were implanted in the gluteal muscles of Sprague-Dawley rats, and the rats were killed after 24 mo and examined for tumors. The following alloys were tested: stainless steel 316L, wrought vitallium, cast vitallium, RMI, unalloyed titanium, $MP_{35}N$ and titanium 6 Al-4V. Three control groups of rats were used: one with no surgery, one in which a sham operation was performed, and one in which a Silastic rad was implanted. A total of 260 animals were used for the study. There were no statistically significant differences in tumor incidence among the alloy implant and control groups. (16 refs.)

77-3822 **Expert Opinions on and Therapeutic Findings in Vine Sprayers of the Moselle Region with Delayed Lesions Caused by Arsenic Poisoning.** (Ger.) Grobe, J. W. (Grabenstrasse 16, 5500 Fier, W. Germany) *Berufsdermatosen* 25(3): 124-130; 1977.

From 1972 to 1976, 122 vine sprayers were examined and treated for delayed toxic effects due to arsenic poisoning. Twenty-two of these cases were first observed in 1976. Av exposure was 20 yr; however, in some patients damage was observed after only 2-4 yr of exposure. Skin melanosis, keratosis, and carcinoma appeared after an av of 26 yr. The sprays involved, Silesia green and Urania green, were used for 30 days/yr, resulting in inhalation doses of 3-30 mg arsenic/day. Comparison of treated and untreated groups showed that the incidence of cancer could be reduced by treatment. Therapy consisted of keratolytic treatment, excision, cauterization, and x-ray irradiation. Of the 122, 8 died in the last 1.5 yr of the following causes: 2 of apoplexy, 3 of lung cancer, and 1 each of cardiac decompensation, arterial sclerosis, and myocardial infarct, all with acrocyanosis. A group of 15 treated patients were compared with 15 untreated patients, with the treated group averaging 70 yr of age and 19 yr exposure and the untreated group, 69 and 18 yr, respectively. The results indicate that over the years 1972-1976, the untreated group had 533 precancerous lesions, the treated group 294. Correspondingly, the untreated group had 3 Bowen's disease foci (compared with 2 in the treated group), 70 basal cell carcinomas (2, untreated group) and 33 spinaliomas (2, untreated group). (14 refs.)

77-3823 **Effect of Diethylstilbestrol on the Cell Kinetics of Subcutaneous Growth of Diethylstilbestrol-induced Renal Carcinoma.** (Eng.) Kaku, K. (Third Dept. Internal Medicine, 1144 Kogushi, Ube 755, Japan) *Gann* 68(3): 315-320; 1977.

Male Syrian hamsters inoculated sc with 3×10^3 cells of a diethylstilbestrol (DES)-induced renal carcinoma were given repeated sc injections of 0.06 mg DES in sesame oil. The growth of the sc tumor in DES-treated and untreated animals was compared with respect to the growth curve, cell cycle time (Tc), growth fraction (GF), and cell loss factor (ϕ). In both groups, tumor growth followed the Gompertz curve, but the latent period was 14 days longer without DES than with DES. In the untreated animals Tc was 80% longer because of prolongation of the G_1 and S phases. However, ϕ was not changed significantly and GF tended to increase without DES. It is concluded that the DES dependency of tumor growth was manifested in the prolongation of Tc. (27 refs.)

77-3824 **Influence of Estrogens on Carcinoembryonic Antigen Levels in the Serum of Rats with Intes-**

tinal Neoplasms and Nonspecific Intestinal Mucosa Injuries. (Rus.) Okulov, V. B. (N. N. Petrov Res. Inst. Oncology, USSR Ministry Public Health, Leningrad, USSR) Anisimov, V. N.; Pozharisski, K. M. *Biull Eksp Biol Med* 83(5): 582-583; 1977.

Carcinoembryonic antigen (CEA) was present in 70% of rats with tumors of the large intestine induced by 1,2-dimethylhydrazine and in rats undergoing posttraumatic regeneration of the intestinal mucosa. After treatment with diethylstilbestrol propionate (0.57 μg/day for 6 days), the frequency of CEA in the sera of these rats was increased. In rats with an injured mucosa of the large intestine, estrogen treatment prevented the natural decrease of CEA during the decline of regeneration. (6 refs.)

77-3825 **Hepatoblastoma in an Infant After Contraceptive Intake During Pregnancy (Letter to Editor).** (Eng.) Otten, J. (Free Univ. Brussels, Brussels 1000, Belgium) Smets, R.; de Jager, R.; Gerard, A.; Maurus, R. *N Engl J Med* 297(4): 222; 1977.

A report is presented of a 7-mo-old boy with an inoperable mixed type hepatoblastoma. The mother had taken 30 μg/day of 18-methyl-norethisterone (Norgestrel) during the first 3 mo of pregnancy. Family history did not provide a definite clue to the etiology of this tumor. (2 refs.)

77-3826 **Medroxyprogesterone Administration in Female Marsh Mice (Meeting Abstract).** (Eng.) Bischoff, F. (Cottage Hosp. Res. Inst., Santa Barbara, CA 93105) Bryson, G. *Proc Am Assoc Cancer Res* 18: 3; 1977. (no refs.)

77-3827 **Unscheduled DNA Synthesis Induced in Hepatocellular Suspensions and Primary Cultures of Hepatocytes by Procarcinogens (Meeting Abstract).** (Eng.) Michalopoulos, G. (Dept. Pathology, Univ. Wisconsin, Madison, WI 53706) Sattler, G. L.; O'Connor, D.; Pitot, H. C. *Proc Am Assoc Cancer Res* 18: 246; 1977. (no refs.)

77-3828 **Survey of Tumor-Producing Agents for Their Ability to Induce Macromolecular Complexes (Meeting Abstract).** (Eng.) Kubinski, H. (Univ. Wisconsin, Madison, WI 53706) Zeldin, P. E.; Morin, N. R. *Proc Am Assoc Cancer Res* 18: 16; 1977. (no refs.)

See also:

* (Rev.): 77-3601, 77-3602, 77-3604, 77-3605, 77-3606, 77-3607, 77-3608, 77-3609, 77-3610, 77-3611, 77-3613, 77-3614, 77-3615, 77-3616, 77-3617, 77-3618, 77-3619, 77-3620, 77-3621, 77-3622, 77-3623, 77-3624, 77-3625, 77-3626, 77-3627, 77-3628, 77-3629, 77-3630, 77-3631, 77-3632, 77-3633, 77-3634, 77-3635, 77-3636, 77-3637, 77-3638, 77-3639, 77-3640, 77-3641, 77-3642, 77-3643, 77-3672, 77-3674, 77-3675, 77-3681, 77-3684, 77-3686, 77-3687, 77-3688, 77-3689, 77-3690, 77-3697, 77-3698, 77-3699, 77-3700, 77-3701.
* (Phys.): 77-3837, 77-3847, 77-3848.
* (Viral): 77-3926, 77-3949, 77-3951.
* (Immun.): 77-3967, 77-3977, 77-3981, 77-3982, 77-3991, 77-4000, 77-4021, 77-4027.
* (Path.): 77-4047, 77-4048, 77-4052, 77-4064, 77-4069, 77-4070, 77-4075, 77-4081, 77-4089, 77-4090, 77-4097, 77-4106.
* (Epid.-Biom.): 77-4141, 77-4143, 77-4147, 77-4148, 77-4150, 77-4152, 77-4153.

PHYSICAL CARCINOGENESIS

77-3829 **Experimental Carcinogenesis in the Rat Thyroid Follicular and C Cells. A Comparison of the Effect of Variation in Dietary Calcium and of Radiation.** (Eng.) Triggs, S. M. (Dept. Pathology, Welsh Natl. Sch. Medicine, Heath Park, Cardiff, CF4 4XN, Wales) Williams, E. D. *Acta Endocrinol (Kbh)* 85(1): 84-92; 1977.

The effect of radiation and of changes in dietary calcium on the development of thyroid tumors was studied in male and female Wistar rats. Three hundred rats were given 0, 5, or 10 μCi of ^{131}I in their first day of life. At 28 days, the rats were weaned onto a low, normal, or high calcium diet. The animals were killed at intervals up to 27 mo of age, and the numbers and kinds of thyroid tumors were recorded. Follicular and C-cell tumors were first seen at 9 mo, and their frequency increased steadily with age. The effect of radiation was highly significant; only 1/41 follicular tumors and 4/22 C-cell tumors occurred in nonirradiated animals. There was a small increase in the frequency of follicular tumors in the high-calcium-diet group compared to the low-calcium group. No significant variation in the frequency of C-cell tumors occurred in relation to dietary calcium. It is concluded that an increase in dietary calcium may be important in the carcinogenesis of follicular but not C-cell tumors and that radiation, known to be carcinogenic for thyroid follicular cells, is also carcinogenic for C cells. (21 refs.)

77-3830 **Studies of Bone and Soft-Tissue Tumours Induced in Rats with Radioactive Cerium Chloride.** (Eng.) Klein, B. (Departement de Virologie, Institut de Cancerologie et d'Immunogenetique, 14 Ave. Paul-Vaillant-Couturier, 94800 Villejuif, France) Pals, S.; Masse, R.; Lafuma, J.; Morin, M.; Binart, N.; Jasmin, J. R.; Jasmin, C. *Int J Cancer* 20(1): 112-119; 1977.

A colloidal suspension of radioactive cerium chloride was injected into the hind legs of Sprague Dawley rats. Bone and soft-tissue tumors were induced at the inoculation site in 77% of the animals. All bone tumors were osteogenic osteosarcomas. Soft tissue tumors were mostly malignant and were of various histological types, predominantly fibrosarcomas, hemangiopericytomas, angiosarcomas, and rhabdomyosarcomas. A kinetic study showed that the doubling time (DT) of the tumors was closely correlated with the anatomical site of tumor development. Bone tumors had a DT of 17.4 days and malignant soft tissue tumors had a DT ranging from 7.4 to 8.4 days, except for two hemangiosarcomas that had a long DT of 17 days. Pulmonary metastases were frequent for osteosarcomas and tumors of vascular origin. This model of induction of bone and soft-tissue tumors in rats by injection of a colloidal suspension of radioactive cerium chloride may be a useful model for studying the kinetics of their human counterparts. (16 refs.)

77-3831 **Biochemical Effects of Inhaled $^{239}\mathrm{PuO}_2$ on Lung Lipids.** (Eng.) Tombropoulos, E. G. (Nutritional Science Branch, Food and Drug Admin., 200 C St. S.W., Washington, DC 20204) Hadley, J. G.; Thomas, J. M.; Craig, D. K. *Health Phys* 32(2): 111-113; 1977.

To assess the effect of the α irradiation associated with plutonium on lung lipid biosynthesis, rats were exposed to $^{239}\mathrm{PuO}_2$. The incorporation of palmitate into lipids was significantly enhanced following medium (23 and 42 nanoCi) and high (more than 100 nanoCi) lung deposition of inhaled $^{239}\mathrm{PuO}_2$. The labeling of palmitate showed that the initial and/or final lecithin pool sizes were different, transfer rates between blood and lung were affected, and rates of degradation of lung lavage lecithin were affected. (4 refs.)

77-3832 **Characteristics of Scinticamera Type Lung Monitor for the Assessment of Plutonium or Uranium in Lungs (Meeting Abstract).** (Eng.) Shirotani, T. (Japan Atomic Energy Res. Inst., Tokai-mura, Naka-gun, Ibaraki-ken 319-11, Japan) Fujita, M.; Mizushita, S. *Health Phys* 33(2): 158; 1977. (no refs.)

77-3833 **Thorotrast-induced Renal Tumours After Retrograde Pyelogram.** (Eng.) Almgard, L. E. (Regionsjukhuset, S-581 85 Linkoping, Sweden) Ahlgren, L.; Boeryd, B.; Slezak, P.; Varenhorst, E. *Eur Urol* 3(2): 69-72; 1977.

The case histories of seven patients with thorotrast kidneys are described. Thorotrast kidneys contain deposits of thorotrast (a 25% colloidal solution of thorium dioxide) resulting from its use for retrograde pyelograms from 1932 to 1952. Of the seven patients, cancer of the kidney developed in five 14-41 yr after the pyelogram. Four of the cancers were obvious renal pelvic carcinomas. It is concluded that there is a high risk of malignancy in connection with thorotrast kidneys. Patients identified as having thorotrast kidneys should be followed up with an iv pyelogram and exfoliative cytology from the renal pelvis. (16 refs.)

77-3834 **Carcinoma of the Bladder after Thorotrast Pyelography.** (Ger.) Schoen, U. (Zentrum fur Pathologie am Klinikum der Justus-Liebig-Universitat, Langhansstrasse 10, 6300 Giessen, W. Germany) Braun, R. *Aktuel Urol* 8(4): 181-5; 1977.

The first case report of a thorotrast-induced carcinoma of the bladder, in a 60-yr-old woman, is presented. The patient had received retrograde pyelography using thorotrast 29 yr prior to discovery of a papilloma in the left ureterostium that, 5 yr later, developed into a carcinoma infiltrating the bladder wall. Numerous thorotrast granules were found in the tumor. Carcinomas of the kidney and pelvis of the kidney induced by thorotrast are known. No data on the minimum dosage necessary for induction are available, but thorotrast, once incorporated in an organ, is not eliminated. No latency limits have been ascertained, but the danger of an induced tumor is constantly present. (11 refs.)

77-3835 **Tumor Induction by Ionizing Radiation.** (Ger.) Schmitt, G. (Strahlenklinik Universitatsklinikum Essen, Hufelandstrasse 55, 43 Essen 1, W. Germany) Littmann, K. *Strahlentherapie* 153(8): 538-542; 1977.

Seven females (8-80 yr old) developed malignant tumors 3-51 yr after radiation therapy with doses of 2,000 to 9,000 rads. The tumors were located within the areas irradiated, and they included 1 basal cell carcinoma, 1 lymphangiohemangiosarcoma, 2 fibrosarcomas, 2 chondrosarcomas, and 1 osteogenic sarcoma. The criteria for radiation induction are that no previous histologically comparable tumor had occurred in the radiation area, that the tumor developed within the radiation area, and that there had been a relatively long symptom-free interval. There is no known threshold dosage, but increasing radiation dosages increase the chances for tumor induction. (19 refs.)

77-3836 **Exposure of Either Parent to Diagnostic Radiation Prior to Conception Produces Serious Genetic Damage in the Child (Meeting Abstract).** (Eng.) Bross, I. D. (Roswell Park Memorial Inst., Buffalo, NY 14263) Natarajan, N. *Proc Am Assoc Cancer Res* 18: 1; 1977. (no refs.)

77-3837 **The Effect of a Stationary Magnetic Field on Induced Carcinogenesis.** (Rus.) Kogan, A. Kh. (Dept. Pathological Physiology, I. M. Sechenov First Moscow Medical Inst., Moscow, USSR) Kulitskaia, V. I. *Patol Fiziol Eksp Ter* (2): 63-68; 1977.

The effect of a stationary magnetic field (350 oersteds) on chemical carcinogenesis was studied in 330 random-bred male rats. Two carcinogens were tested: benzo(a)pyrene (BP) and polyvinyl chloride (PVC). Magnetic plates covered with BP or a PVC film were implanted sc; control animals were exposed to Duralumin plates covered with the respective carcinogen. The magnetic field increased the latent period from 3 mo, 3 wk to 4 mo, 2 wk for the BP-induced tumors and from 12 to 13.5 mo for the PVC-induced tumors. In the magnetic field, 21/25 rats developed BP-induced tumors (compared to 21/23 controls) and 14/52 rats developed PVC-induced tumors (compared to 17/50 controls). The magnetic field enhanced tumor growth and increased the incidence of poorly differentiated (polymorphocellular) sarcomas from 29.4% to 50% for BP-induced tumors and from 9.5% to 19.5% for PVC-induced tumors. (38 refs.)

77-3838 **Chronic Effects of 375-MeV/Nucleon Cyclotron-Accelerated ^{20}Neon Ions (Meeting Abstract).** (Eng.) Woodruff, K. H. (Univ. California, Berkeley, CA 94720) Leith, J. T.; Havens, V.; Smith, P.; Lyman, J.; Howard, J.; Tobias, C. A. *Am J Pathol* 86(2): 71a; 1977. (no refs.)

77-3839 **Immunofluorescent Studies of Epidermal Protein During UV Induced Carcinogenesis.** (Eng.) Hersh, L. (Dept. Dermatology, Univ. California Sch. Medicine, San Francisco, CA 94143) Fukuyama, K.; Inoue, N.; Epstein, J. H. *Virchows Arch (Cell Pathol)* 24(2): 157-164; 1977.

Previous agar diffusion studies demonstrated that antibodies produced in rabbits by injection of urea-extractable proteins of rat cornified cells cross-react with proteins extracted from normal epidermis of hairless mice using the same technique. In the present study, the immunoreactivity of epidermal proteins in hyperplasia and malignant transformation induced by UV rays between 280-320 nanometers (UVB) was investigated by indirect immunofluorescence microscopy. Reactivity to the antibody was seen over the entire epidermis of untreated skin and hypertrophied epidermis; it occurred 6-8 wk after the initiation of UVB irradiation. However, the reactivity diminished when malignant changes took place in the epidermal cells. The immunoresponse almost disappeared completely in squamous cell carcinoma produced by further UVB radiation. These results suggest that the reactivity of this urea-extractable protein serves as an additional immunologic marker for normal epidermal cells. Alterations in immunoreactivity parallel UVB-induced carcinogenesis. (18 refs.)

77-3840 **Modification of Immunological Potential by Ultraviolet Radiation. I. Immune Status of Short-Term UV-irradiated Mice.** (Eng.) Spellman, C. W. (Dept. Pathology, Univ. Utah Medical Center, Salt Lake City, UT 84132) Woodward, J. G.; Daynes, R. A. *Transplantation* 24(2): 112-119; 1977.

C3H/HeN mice support the progressive growth of most transplanted syngeneic UV light-induced tumors following short-term UV exposure, whereas nonexposed mice reject these tumors. To determine whether UV irradiation renders mice tumor susceptible by causing general immunosuppression, several immunological parameters were compared. These include antibody production, proliferation in response to antigenic and mitogenic stimulation, and the generation of cytotoxic effector cells by normal or short-term UV-exposed mice. The results indicate that short-term UV irradiation (6.6×10^5 ergs/cm^2, 30 min/day, 5 times/wk for 5 wk) of mice does not result in any readily detectable alterations of the host's immune system other than consistent loss of the antitumor response mediating rejection of the transplanted UV-induced tumor. (19 refs.)

77-3841 **Modification of Immunological Potential by Ultraviolet Radiation. II. Generation of Suppressor Cells in Short-Term UV-irradiated Mice.** (Eng.) Spellman, C. W. (Dept. Pathology, Univ. Utah Medical Center, Salt Lake City, UT 84112) Daynes, R. A. *Transplantation* 24(2): 120-126; 1977.

When normal C3Hf/HeN mice are exposed for short periods to UV light, they support the progressive growth of transplanted syngeneic UV-induced tumors. Normal nonirradiated mice almost always reject these tumor implants. The UV-mediated suppression of the antitumor response could be adoptively transferred to normal syngeneic mice with lymphoid cells derived from short-term UV-irradiated donors. Transfer of the suppressive effect was dose-dependent and appeared to require the presence of viable T lymphocytes. Suppressive activity was observed in both the spleen and thymus of UV-irradiated donors. In a preceding study, it was established that thymus UV irradiation does not cause a general depression of testable immune functions. Collectively, these data suggest that short-term UV irradiation of mice increases suppressor cell activity, thereby inhibiting the host's ability to respond to an antigenic UV-induced tumor. The possible role of this phenomenon in UV carcinogenesis is discussed. (7 refs.)

77-3842 **Resident Population of Germinal Cells of 5.5-Day-Old Chick Embryos after Irradiation of the Young Blastoderms with UV Rays.** (Fre.) Reynaud, G. (Laboratoire de Morphogenese experimentale et Caryologie Universite de Provence 3, place Victor-Hugo, 13331 Marseille, Cedex 3, France) *CR Acad Sci [D] (Paris)* 284(10): 843-846; 1977.

The effect of UV irradiation of the chick blastoderm on primordial germ cells is discussed. A mineralight SL 2537 lamp was used to direct 2,537-A UV irradiation at doses of 14,400 and 16,200 ergs/mm^2 to 5-hr white Leghorn chick embryos in windowed eggs. After 5.5 days, very few or no germ cells were observed in the primordial gonad. It is concluded that total irradiation of the young chick blastoderm has a definite effect on the developing gonad in the 5.5-day-old chick. Unfortunately, the dose that produces complete sterilization (16,200 ergs/mm^2) is not compatible with normal development of the chick. (16 refs.)

77-3843 **Facilitation of Nodal Metastasis from a Nonimmunogenic Murine Carcinoma by Previous Whole-Body Irradiation of Tumour Recipients.** (Eng.) Hewitt, H. B. (C.R.C. Gray Lab., Mount Vernon Hosp., Northwood, Middlesex HA6 2RN, England) Blake, E. R. *Br J Cancer* 36(1): 23-34; 1977.

Of 193 CBA mice kept under prolonged observation after excisions of small id transplants of a nonimmunogenic tumor (CBA carcinoma NT), 27 presented with local recurrence, 19 with regional lymph-nodal metastasis (RNM), and 72 with pulmonary metastasis, with or without other systemic metastases. When mice were exposed to sublethal whole-body irradiation (WBI, 600 rads) before tumor transplantation, the incidence of RNM rose to approx 80% and the mean latent period was reduced from 60 days to 40 days after tumor transplantation. This enhancement of RNM by WBI was undiminished when the interval between WBI and tumor transplantation was increased from 1 to 90 days. An explanation for this effect in terms of immunosuppression by the WBI is unlikely for the following reasons: the tumor was nonimmunogenic by standard quantitative tests; the effect persisted long after the expected time for recovery of immune reactivity; and iv injection of normal marrow and lymphoid cells after WBI failed to reduce the effect. That the effect was systemic was proved by failure of local preirradiation of the tumor bed or regional node to enhance RNM. The effect was not observed when WBI was given 4 days after tumor excision. These and other experiments failed to indicate the mechanism of the effect of WBI, but its long persistence suggests that it may relate to stored lethal radiation damage in migrating cells of slow turnover tissues. (16 refs.)

77-3844 **X-Ray Exposure and Premature Aging.** (Eng.) Bertell, R. (Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263) *J Surg Oncol* 9(4): 379-391; 1977.

A hypothesis of an aging effect of exposure to ionizing radiation in humans is proposed and given precise mathematical expression. It is assumed that the biological changes occurring in humans exposed to ionizing radiation from medical x-rays are comparable to those occurring through natural aging, since both factors increase the relative risk of nonlymphatic leukemia. The assumption focuses on this one aspect of aging only. The hypothesis that aging and ionizing radiation increase the relative risk of nonlymphatic leukemia similarly is tested against data from the Tri-State Leukemia Survey. The data are explained in a statistically acceptable way, giving an estimate of 1 rad skin dose exposure to the trunk as comparable to 1 yr of natural aging. This research raises further questions about the effects of exposure to ionizing radiation and presents a new methodology by which these questions may be researched. (14 refs.)

77-3845 **Squamous Cell Carcinoma Appearing in X-Ray-treated Mycosis Fungoides.** (Eng.) Volden, G. (Dept. Dermatology, Rikshospitalet, Oslo, Norway) Larsen, T. E. *Acta Derm Venereol (Stockh)* 57(4): 341-343; 1977.

Two men (aged 62 and 60 yr, respectively) with mycosis fungoides developed squamous cell carcinoma on the neck. After verification by routine biopsy of material from a suppurating infiltrate of the neck, both patients were treated intermittently with x-rays. Both had developed the carcinoma on a sun-exposed area. Patient 1 was treated with Grenz rays [10 kilovolts (kV)] totaling 4,400 rads, and Dermopan Step IV (50 kV), 5,200 rads. Patient 2 received Grenz rays, 4,600 rads; Dermopan Step IV, 4,000 rads; and soft x-rays (150 kV), 800 rads. The latency period was, respectively, 3 and 10 yr. (4 refs.)

77-3846 **Struma Maligna after X-Ray Irradiation of the Neck.** (Ger.) Valesky, A. (Chirurgische Klinik der Universitat Munchen, Nussbaumstrasse 20, 8000 Munich 2, W. Germany) Spelsberg, F. *Strahlentherapie* 153(8): 543-544; 1977.

A parotid gland carcinoma was excised from a 24-yr-old patient, and the neck region was irradiated with 6,000 rads. A papillary thyroid gland carcinoma was removed 4 yr later. The connection between exposure of the thyroid gland to radiation and formation of the carcinoma is discussed. (15 refs.)

77-3847 **Enhancement of DMBA Carcinogenesis in Hamster Cheek Pouch by Repeated Localized Low-Level X-Irradiation (Meeting Abstract).** (Eng.) Lurie, A. G. (Univ. Connecticut Health Center, Farmington, CT 06032) *Proc Am Assoc Cancer Res* 18: 4; 1977. (no refs.)

77-3848 **Leukemogenesis in Mice by 3-Methylcholanthrene (MCA) and by X-Irradiation: Association of Irradiation Leukemia with Induction of Endogenous Ecotropic Murine Leukemia Virus (Meeting Abstract).** (Eng.) Comas, C. (Albert Einstein Coll. Medicine, Bronx, NY 10461) Mayer, A.; Bosch, A.; Duran-Reynals, M. L. *Proc Am Assoc Cancer Res* 18: 47; 1977. (no refs.)

77-3849 **Trisomy of Chromosome 15 in X-Ray-Induced Mouse Leukemia (Meeting Abstract).** (Eng.) Chang, T. D. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021) Biedler, J. L.; Stockert, E.; Old, L. J. *Proc Am Assoc Cancer Res* 18: 225; 1977. (no refs.)

77-3850 **Leukemia and Lymphoma in Irradiated Parabiont Rats (Meeting Abstract).** (Eng.) Warren, S. (Cancer Res. Inst., New England Deaconess Hosp., boston, MA 02215) Chute, R. N.; Porter, M. W.; Brown, C. E.; Gates, O. *Radiat Res* 70(3): 606; 1977. (no refs.)

77-3851 **Carcinoma of the Prostate in Irradiated Parabiotic Rats (Meeting Abstract).** (Eng.) Brown, C. E. (Cancer Res. Inst., New England Deaconess Hosp., Boston, MA 02215) Warren, S. *Proc Am Assoc Cancer Res* 18: 51; 1977. (no refs.)

77-3852 **ENDOR Study of an Allyl Radical in Deoxycytidine 5'-Phosphate: Radical Formation and**

Biological Implications (Meeting Abstract). (Eng.) Fouse, G. W. (Dept. Radiation Biology and Biophysics, Univ. Rochester, Rochester, NY 14642) Close, D. M.; Bernhard, W. A. *Radiat Res* 70(3): 615; 1977. (no refs.)

77-3853 **DNA Repair in Human Lymphocytes (Meeting Abstract).** (Eng.) Agarwal, S. S. (Inst. Cancer Res., Fox Chase, Philadelphia, PA 19111) Brown, D. Q. *Proc Am Assoc Cancer Res* 18: 32; 1977. (no refs.)

77-3854 **DNA Strand Break Induction and Rejoining in Chinese Hamster Cells as a Function of Radiation Quality (Meeting Abstract).** (Eng.) Ritter, M. A. (Univ. California, Berkeley, CA 94720) *Diss Abstr Int [B]* 37(9): 4347; 1977. (no refs.)

77-3855 **Early Detection of Spontaneous Neoplastic Transformation In Vitro of Mouse Connective Tissue (CT) Using Implants of Cells Attached to Small Plastic Plates (Meeting Abstract).** (Eng.) Boone, C. W. (NCI, Bethesda, MD 20014) Takeichi, N. *Proc Am Assoc Cancer Res* 18: 173; 1977. (no refs.)

77-3856 **From Uterus to Petri Dish: Transformation In Utero and In Vitro (Meeting Abstract).** (Eng.) Borek, C. (Columbia Univ., New York, NY 10032) Pain, C. *Radiat Res* 70(3): 649-650; 1977. (no refs.)

See also:

* (Rev.): 77-3601, 77-3603, 77-3609, 77-3612, 77-3636, 77-3644, 77-3645, 77-3646, 77-3674, 77-3683.
* (Chem.): 77-3821.
* (Viral): 77-3926, 77-3946.
* (Path.): 77-4051, 77-4070, 77-4077, 77-4081, 77-4095.
* (Epid.-Biom.): 77-4149, 77-4153.

VIRAL CARCINOGENESIS

77-3857 **Pseudotypes of Vesicular Stomatitis Virus with the Mixed Coat of Reticuloendotheliosis Virus and Vesicular Stomatitis Virus.** (Eng.) Kang, C. Y. (Dept. Microbiology, Univ. Texas Health Science Center, Southwestern Medical Sch., Dallas, TX 75235) Lambright, P. *J Virol* 21(3): 1252-1255; 1977.

The ability of vesicular stomatitis virus (VSV) to form pseudotypes with envelope components of reticuloendotheliosis virus (REV) is reported. The VSV pseudotype possessed the limited host range and antigenic properties of REV. Approx 70% of VSV, Indiana serotype, and 45% of VSV, New Jersey serotype, produced from the REV strain T-transformed chicken bone marrow cells contained mixed envelope components of both VSV and REV. VSV pseudotypes with mixed envelope antigens were neutralized with excess amounts of either anti-VSV antiserum or anti-REV antiserum. (11 refs.)

77-3858 **Characterization of DNA Complementary to Nucleotide Sequences Adjacent to Poly(A) at the 3′-Terminus of the Avian Sarcoma Virus Genome.** (Eng.) Tal, J. (Ben Gurion Univ. Negev, Faculty Natural Sciences, Dept. Biology, Beersheva 84 120, Israel) Kung, H. J.; Varmus, H. E.; Bishop, J. M. *Virology* 79(1): 183-197; 1977.

DNA (cDNA) complementary to a sequence of 300-400 nucleotides adjacent to the poly(A) at the 3′-terminus of the genome of avian sarcoma virus (ASV) was prepared. DNA was transcribed from denatured ASV RNA following initiation on the primer $(dT)_{12-18}$. Homopolymer synthesis was n a significant feature of the enzymatic reaction, and most if not all the initiations on $(dT)_{12-18}$ occurred at or near the 3′-terminus of the viral RNA. The presence of oligo(dT) on $cDNA_{3}{}'$ accelerates hybridization between $cDNA_{3}{}'$ and polyadenylated viral RNA; this artifact can be eliminated by including a competing homopolymer [poly(dT) or poly(A)] in the reaction mixtures. Nucleotide sequences complementary to $cDNA_{3}{}'$ occur only once or twice in the genome of ASV, are present in the genomes of virus strains from subgroups A, B, C, D, E, and F of avian leukosis-sarcoma viruses, and are conserved even when large deletions affect an adjacent viral gene (*src*). By contrast, there is little or no complementarity between $cDNA_{3}{}'$ and the genomes of golden pheasant virus (subgroup G of avian leukosis-sarcoma viruses), mouse mammary tumor virus, and the Moloney strains of murine sarcoma virus and murine leukemia virus. $cDNA_{3}{}'$ can be used to identify the 3′-terminus of the ASV genome by molecular hybridization and will, therefore, be a useful reagent for the analysis of viral replication. (51 refs.)

77-3859 **Properties of Mammalian Cells Transformed by Temperature-sensitive Mutants of Avian Sarcoma Virus.** (Eng.) Chen, Y. C. (Dept. Microbiology, Univ. Southern California Sch. Medicine, 2025 Zonal Ave., Los Angeles, CA 90033) Hayman, M. J.; Vogt, P. K. *Cell* 11(3): 513-521; 1977.

Fibroblasts from the European field vole (*Microtus agrestis*) and from normal rat kidney (NRK) were infected with avian sarcoma virus (ASV) mutants that are temperature-sensitive (ts) for the maintenance of transformation. These cells were transformed at 33 C, but showed normal cell characteristics in morphology, colony formation in agar, saturation density, sugar uptake, and membrane proteins at 39 C and 40 C, the nonpermissive temperatures. Ts mutant virus was rescued from most of the ts-transformed cell lines. NRK cells infected by ASV ts mutants and kept at the nonpermissive temperature could be transformed by wild-type ASV. The susceptibility of the ts-transformed NRK lines to this transformation was higher than the susceptibility of uninfected NRK at either the permissive or nonpermissive temperature. Possible explanations of this enhanced susceptibility are discussed. (37 refs.)

77-3860 **Influence of Age at Inoculation on Avian Oncornavirus-induced Brain Tumor Incidence, Tumor Morphology, and Postinoculation Survival in F344 Rats.** (Eng.) Copeland, D. D. (Dept. Pathology, Duke Univ. Medical Center, Durham, NC 27710) Bigner, D. D. *Cancer Res* 37(6): 1657-1661; 1977.

The incidence and histology of brain tumors and survival were determined in F344 rats inoculated at various ages with an intracerebral inoculum of 87,000 focus-forming units of Bratislava-77 strain avian sarcoma virus. Brain tumors arose in all animals inoculated at ages 1 day, 9 days, and 97-99 days and in 20/30 inoculated at age 528 days. Survival time increased with increasing age at inoculation: mean survival times were 83.8, 173.5, and 290.7 days in 1-, 9-, and 97- to 99-day-old rats, respectively. The mean incidence of multiple tumors declined with increasing age at inoculation, being 3.09, 1.51, and 1.07 tumors/animal in the 1-, 9- and 97- to 99-day animals, respectively. Poorly differentiated astrocytomas of mixed morphology were common among rats inoculated as neonates; solitary pilocytic astrocytomas were the most common tumors among rats inoculated as adults. This is consistent with a shift in the maturity of cells transformed, from the poorly differentiated subependymal cell in the neonate to the more mature cortical astrocyte in the adult. (26 refs.)

77-3861 **Provirus Genetic Material of Rous Sarcoma Virus in Mammalian Tumor Cells.** (Rus.) Farashian, V. R. (D. I. Ivanovskii Inst. Virology, Acad. Medical Sciences USSR, Moscow, USSR) Obukh, I. B.; Serov, S. M.; Zhdanov, V. M. *Dokl Akad Nauk SSSR* 234(1): 203-206; 1977.

The characteristic features of provirus genetic material were studied in nonvirogenic mice RVP_3 and rat TWERC cells and virogenic rat XC cells induced by Rous sarcoma virus (RSV). The DNA and RNA fractions isolated from virogenic and nonvirogenic cells were hybridized with ^3H-DNA transcripts of RSV from RSV-induced tumors in chickens. Virus-specific DNA was integrated into the genome in all three types of cells. The relative content of virus-specific DNA in the RVP_3 and TWERC cells was less than that in the XC cells (70%, 88%, and 100%, respectively). (10 refs.)

77-3862 **Coordinate Control of Collagen Synthesis and Cell Growth in Chick Embryo Fibroblasts and the Effect of Viral Transformation on Collagen Synthesis.** (Eng.) Kamine, J. (Biology Dept. Massachusetts Inst. Technology, Cambridge, MA 02139) Rubin, H. *J Cell Physiol* 92(1): 1-11; 1977.

Purified protease-free collagenase was used to determine the rate of ^3H-proline incorporation into collagen polypeptides in partially synchronized secondary cultures of chick embryo fibroblasts (CEF). The rate of collagen synthesis remained a constant fraction of the overall protein synthesis (5%) regardless of cell growth rate, even when the rate of protein synthesis was accelerated five-fold by adding serum and altering the pH of the culture medium. However, in cells oncogenically transformed by Rous sarcoma virus (RSV) the relative rate of collagen synthesis decreased by 50% 24 hr after infection and was 10% of the initial rate after 5 days. This selective decrease could be reversed in cells infected with an RSV temperature-sensitive transformation-defective mutant at the nonpermissive temperature, indicating that it was not merely the result of viral infection but was a direct consequence of oncogenic transformation. (32 refs.)

77-3863 **Terminal Redundancy and the Origin of Replication of Rous Sarcoma Virus RNA.** (Eng.) Coffin, J. M. (Dept. Molecular Biology, Tufts Univ. Sch. Medicine, Boston, MA 02111) Haseltine, W. A. *Proc Natl Acad Sci USA* 74(5): 1908-1912; 1977.

The genomic RNA of Prague B Rous sarcoma virus (RSV) was used as an template for the in vitro synthesis of RSV DNA by virion endogenous RNA-dependent DNA polymerase after initiation on a transfer RNA-trp (tRNA-trp) primer located near the 5′ end of the RNA. A major product was a piece of DNA 101 nucleotides long (strong stop DNA) that could be isolated covalently bound to the tRNA primer. This DNA was complementary to the extreme 5′ end of the RNA. It was also demonstrated that the 5′ and 3′ ends of the RSV genome, excluding the cap and poly(A) portions, have identical sequences 21 nucleotides long. It is proposed that the function of this sequence is to facilitate elongation from the 3′ end of the DNA chains initiated elsewhere on the viral genome. (24 refs.)

77-3864 **Distinguishable Transformation-defective Phenotypes among Temperature-sensitive Mutants of Rous Sarcoma Virus.** (Eng.) Becker, D. (Institut fur Virologie, Fachbereich Humanmedizin, 6300 Giessen, W. Germany) Kurth, R.; Critchley, D.; Friis, R.; Bauer, H. *J Virol* 21(3): 1042-1055; 1977.

Eight transformation-defective, temperature-sensitive (ts) mutants of Prague B Rous sarcoma virus were isolated after mutagenesis with 5-bromodeoxyuridine followed by selection on the basis of focus tests. Five of these mutants, ts GI201, GI202, GI203, GI204, and GI205, are similar to most previously reported isolates in that they show a ts response to a variety of transformation-specific parameters. In addition to the ts defect, GI201 carries a lesion that was observed to be a nonconditional loss of expression of plasminogen activator protease. Three mutants, ts GI251, GI252, and GI253, are partial transformation-defective (PTD) mutants, since they behave as ts mutants in some transformation tests and as wild-type mutants in others. These three mutants fail to form foci at the nonpermissive temperature (41 C) and are non-tumorigenic in 3-wk-old chickens (body temperature, 42 C). The agglutinability by concanavalin A of cells infected with these mutants shows a definite temperature sensitivity, as do the rate of 2-deoxyglucose uptake and the disappearance of the 250,000-dalton normal cell glycoprotein [large, external, transformation-sensitive (LETS)]. Although the PTD mutant-infected cells, unlike cells infected with other transformation mutants, exhibit a cell-bound plasminogen activator protease at the nonpermissive temperature, this activator is not detectable as a free protease in the medium, as it is with wild-type, virus-infected cells. The PTD mutants behave like the wild-type parent in their ability to induce transformed growth properties in the infected cells; ie, growth beyond normal cell saturation density with or without serum-supplemented medium and growth leading to colony formation in soft agar- or methylcellulose-containing suspension media. (48 refs.)

77-3865 **Effect of Temperature on Arginine Incorporation by Ribosomeless Extracts of Cells Transformed By a Temperature-sensitive Mutant of Rous Sarcoma Virus.** (Eng.) Rao, P. (Inst. Cancer Res., Fox Chase Cancer

Center, Philadelphia, PA 19111) Kaji, H. *Biochim Biophys Acta* 477(4): 394-403; 1977.

The effect of transformation of normal rat kidney cells by a temperature-sensitive mutant of Prague strain Rous sarcoma virus (*ts* LA 24 PR-A) on the posttranslation addition of arginine to the NH_2-terminus of preformed acceptor molecules has been studied. Cells maintained at the permissive (35 C) temperature show a high arginine-incorporating activity in ribosome-free extracts compared with that in cell extracts grown at the nonpermissive (40 C) temperature. Temperature-shift experiments as well as studies with cells transformed by wild-type Rous sarcoma virus suggest that the decreased activity in cells grown at 40 C is not due to a high temperature per se. The lower arginine incorporation in the 40 C cell extracts is due partially to a decrease in the activity of arginyl transferase, which catalyses the transfer of arginine from arginyl transfer RNA to the acceptor protein. Polyacrylamide gel electrophoresis of the radioactive product shows that the acceptor molecules in cell extracts grown at 40 C are larger and qualitatively different from those in cell extracts grown at 35 C. (4 refs.)

77-3866 **Decreased Rate of S-Adenosyl-L-homocysteine Metabolism: An Early Event Related to Transformation in Cells Infected with Rous Sarcoma Virus.** (Eng.) Pierre, A. (Institut de Chimie des Substances Naturelles, C.N.R.S., 91190 Gif sur Yvette, France) Richou, M.; Lawrence, F.; Robert-Cero, M.; Vigier, P. *Biochem Biophys Res Commun* 76(3): 813-819; 1977.

The metabolic rates of S-adenosylhomocysteine (SAH) in normal chick embryo fibroblasts (CEF), in Rous sarcoma virus (RSV)-transformed CEF, and in Rous sarcoma-associated virus (RAV_1)-infected (nontransformed) CEF cells were compared. The normal and RAV_1-infected cells degraded SAH at the same rate: 70%-73% of 2 mM SAH in a cell-free extract of the cells disappeared in 1 hr. The RSV-transformed cells degraded SAH at a reduced rate: only 14% of the SAH disappeared in 1 hr. Further investigation demonstrated that there was a significant fall in SAH-hydrolase activity in the RSV-transformed cells compared to the normal or RAV_1-infected cells. There was also a loss of adenosine deaminase activity in the RSV-transformed and RAV_1-infected cells. It is concluded that the failure of SAH to inhibit cell transformation induced by RSV, in contrast to one of its synthetic analogs, 5′-S-isobutyladenosine, does not stem from a more rapid degradation in transformed cells than in normal cells. (16 refs.)

77-3867 **A Very Sensitive Biochemical Assay for Detecting and Quantitating Avian Oncornaviruses.** (Eng.) Tereba, A. (Lab. Virology, St. Jude Children's Res. Hosp., 332 N. Lauderdale, Post Office Box 318, Memphis, TN 38101) Murti, K. G. *Virology* 80(1): 166-176; 1977.

A biochemical assay, only slightly less sensitive than currently used biological assays, was developed to detect and quantitate avian oncornaviruses. The assay, which is based on the unusual stability of most avian oncornavirus RNA-dependent DNA polymerases at 30 C, made it possible to quantitate, with an error of ±10%, as few as 1,000 Rous sarcoma or Rous-associated virions directly in the tissue culture medium. Lower limits of detection for golden pheasant virus and reticuloendotheliosis virus were 3×10^6 virions, respectively. Assay results varied less than fivefold when different strains or subgroups of Rous sarcoma or Rous-associated viruses with virion-to-infectivity ratios of 7 to 1,000 were used. (23 refs.)

77-3868 **Heteroduplex Analysis of Avian RNA Tumor Viruses.** (Eng.) Junghans, R. P. (Dept. Chemistry 164-30, California Inst. Technology, Pasadena, CA 91125) Hu, S.; Knight, C. A.; Davidson, N. *Proc Natl Acad Sci USA* 74(2): 477-481; 1977.

An electron microscope heteroduplex analysis of avian RNA tumor viruses was made by means of 35S viral RNA and long, complementary DNA synthesized in vitro. Heteroduplex molecules were formed between complementary DNA from Rous sarcoma virus Prague B (Pr-B) and RNA's from Pr-B and Rous sarcoma virus Prague C (Pr-C) and from their transformation-defective (td) derivatives td-Pr-B and td-Pr-C. In the case of heteroduplexes with the td viruses, a deletion loop of the order of 2 kilobases in size and < 1 kilobase from the 3′ terminus of the RNA was observed. This deletion probably spans part or all of the sequences of one or more genes in the nondefective sarcoma virus essential for cell transformation. The sizes and the positions of the deletions in the td-Pr-B and td-Pr-C viruses differed slightly but significantly. No features of nonhomology were observed in the Pr-B-Pr-C hybrids, confirming the close genetic relatedness of the two viruses. All heteroduplexes contained a proportion of circular and dimer molecules. This observation is a direct demonstration that (-) strand DNA transcription begins at an internal position of the RNA genome, proceeds to the 5′ end, reinitiates at the 3′ end of the RNA, and copies the remainder of the viral genome. Other implications for models of RNA tumor virus replication are also developed from these data. (25 refs.)

77-3869 **Studies on the Intracellular Reverse Transcriptase of RNA Tumor Viruses.** (Eng.) Panet, A. (Dept. Virology, Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel) *Isr J Med Sci* 13(7): 731-739; 1977.

A radioimmunoassay using antiserum to the reverse transcriptase (RT) of avian myeloblastosis virus (AMV) was used to detect and characterize RT in virions and in virus-infected cells. The principal findings of the study were: (1) RT has no antigenic similarity to any other viral proteins; (2) the RT's of AMV and Rous sarcoma virus are very similar, but differences do occur in a small population of type-specific antigenic determinants; (3) the RT of murine leukemia virus shares no common antigenic determinants with the RT of AMV. Two types of RT were detected in virus-producing cells. One type was eluted from phosphocellulose columns in a position identical to that of the RT in mature virions; the other type could be detected by radioimmunoassay but did not bind to phosphocellulose. The latter enzyme made up 50% of the total RT antigen in the cell but possessed low DNA polymerase activity (compared to the former). (23 refs.)

77-3870 **Homogeneity and Complexity of Avian Oncornavirus Proviral DNA Determined by Molecular Hybridization.** (Eng.) Evans, R. M. (Rockefeller Univ., Dept. Molecular Biology, New York, NY 10021) Shoyab, M.; Drohan, W. N.; Baluda, M. A. *J Virol* 21(3): 942-948; 1977.

Single or multistep hybridization was used to demonstrate the homogeneity of DNA complementary to the 35S RNA subunit of avian myeloblastosis virus (AMV). For multistep hybridizations, 35S AMV RNA was preselected for its ability to hybridize either to unfractionated leukemic DNA or to leukemic DNA enriched for unique or reiterated sequences. These experiments indicated that the viral genome is complementary to DNA sequences with a low reiteration frequency. Competition experiments confirmed the absence of fast-hybridizing sequences in viral DNA. Computer analyses of the data revealed that there are two to four copies of viral DNA in infected cells. (36 refs.)

77-3871 **Different Modes of Inhibition of Purified Ribonucleic Acid Directed Deoxyribonucleic Acid Polymerase of Avian Myeloblastosis Virus by Rifamycin SV Derivatives.** (Eng.) Gurgo, C. (Inst. Molecular Virology, St. Louis Univ. Medical Center, St. Louis, MO 63110) Grandgenett, D. P. *Biochemistry* 16(4): 786-792; 1977.

An investigation was made of the ability of several rifamycin SV derivatives to inhibit the purified$\alpha\beta$ RNA-directed DNA polymerase of avian myeloblastosis virus on a poly(A) template. These derivatives included C-27 (rifamycin SV with a dicyclohexylalkyl-substituted piperidyl ring at the 3 position), AF-013 (O-n-octyloxime of 3-formylrifamycin SV), and AF/DNFI [3-(2,4-dinitrophenylhydrazonemethyl)-rifamycin SV]. Polyacrylamide gel profiles of poly(dt) synthesized in the presence and absence of the drugs were compared. The ability of C-27, AF-013, and AF/DNFI (in order of decreasing activity) to inhibit the viral DNA polymerase at an initial step was directly related to the lipophilicity of the derivatives. When the inhibition of later steps was examined, no such correlation was observed. C-27 was the least inhibitory of the three derivatives toward polymerization per se: analysis of the mode of inhibition demonstrated that reinitiation, not chain elongation, was inhibited. The amount of product synthesized in the presence of C-27 was decreased, but there was no effect on size distribution. Both the amount and the size of product were decreased in the presence of AF-013, suggesting an effect on chain elongation as well as on initiation. Kinetic evidence suggested that AF/DNFI has a mode of action similar to that of AF-013. The results of the study are discussed in terms of different mechanisms of interaction of rifamycin SV derivatives with the viral DNA polymerase. (44 refs.)

77-3872 **Primer Recognition by Avian Myeloblastosis Virus RNA-directed DNA Polymerase.** (Eng.) Brown, R. D. (Dept. Biological Chemistry, Coll. Medicine, Univ. Cincinnati, Cincinnati, OH 45267) Armentrout, R. W. *J Virol* 21(3): 1236-1239; 1977.

To test the specificity of RNA-directed DNA polymerase for the transfer RNA (tRNA) structure, tryptophanyl-tRNA was specifically labeled at the 3′ end with ^{3}H-tryptophan and cleaved in half with RNase under denaturing conditions. The 3′ half hybridized exclusively at the 5′ end of avian myeloblastosis virus RNA. The RNA-dependent DNA polymerase of avian myeloblastosis virus is capable of efficiently binding the 3′ half of the primer molecule. (14 refs.)

77-3873 **tRNAtrp (Bovine) Binding to the Reverse Transcriptase of Avian Myeloblastosis Virus and Function as a Heterologous Primer.** (Eng.) Baroudy, B. M. (Dept. Biochemistry, Sch. Medicine, Georgetown Univ., Washington, DC 20007) Fournier, M.; Labouesse, J.; Papas, T. S.; Chirikjian, J. G. *Proc Natl Acad Sci USA* 74(5): 1889-1893; 1977.

A comparison was made of the abilities of transfer RNA-trp (tRNA-trp) (avian) and tRNA-trp (bovine), which have similar primary structures, to bind to the $\alpha\beta$ form of RNA-dependent DNA nucleotidyltransferase of avian myeloblastosis virus (AMV) and to act as primers for the transcription of 35S RNA from AMV. Both forms of tRNA-trp formed stable complexes with the nucleotidyltransferase. The tRNA-trp (bovine) initiated DNA synthesis on the AMV 35S RNA template. Since it can be obtained in larger amounts than the avian primer, it should be of value for further experimental studies of primer/nucleotidyl-transferase interactions. (33 refs.)

77-3874 **Purification of a Glycoprotein from Bovine Leukemia Virus (BLV).** (Eng.) Frenzel, B. (Federal Res. Inst. Animal Virus Diseases, Tubingen, W. Germany) Kaaden, O. R.; Mussgay, M. *Z Naturforsch* 32c(3/4): 301-304; 1977.

Two-step isoelectric focusing was carried out at pH 3.5-10 and pH 3-6 to isolate a precipitating antigen of bovine leukemia virus (BLV). Serologically active fractions were purified by Sephadex G150 gel filtration and analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The results revealed the presence of a homogeneous protein with a relative molecular wt of 69,000 daltons that was designated BLV gp69. A protein with a similar molecular wt could also be demonstrated in BLV particles. Using an immunodiffusion test, antibodies against gp69 were detected in 34/35 sera from cattle affected by enzootic bovine leukosis, whereas sera from 197 animals with normal lymphocyte numbers showed no reaction. (7 refs.)

77-3875 **Proteins of Bovine Leukemia Virus. I. Characterization and Reactions with Natural Antibodies.** (Eng.) Deshayes, L. (Laboratoire d'Immunologie et de Virologie des Tumeurs-INSERM U152, Hopital Cochin, 75014 Paris, France) Levy, D.; Parodi, A. L.; Levy, J. P. *J Virol* 21(3): 1056-1060; 1977.

Bovine leukemia virus (BLV) was purified from a chronically infected fetal lamb kidney cell line. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of this virus revealed the presence of eight distinguishable viral components with molecular wt of 80,000 to 11,000. The major component is a nonglycosylated protein with a molecular wt of 24,000 (p24). At least three heavier polypeptides were found, one of them representing a glycoprotein (gp60). In addition, four minor polypeptides with respective molecular wt of 19,000, 16,000, 13,000, and 11,000 were identified. In a complement fixation assay using naturally occurring antibodies of a leukemic cow, four polypeptides (gp 60, p35, p24, and p16) were found to be reactive. (26 refs.)

77-3876 **Bovine Papilloma Virus: Presence of Virus-specific DNA Sequences in Naturally Occurring Equine Tumors.** (Eng.) Lancaster, W. D. (Dept. Veterinary Science, Univ. Wisconsin, Madison, WI 53706) Olson, C.; Meinke, W. *Proc Natl Acad Sci USA* 74(2): 524-528; 1977.

Four of five spontaneous benign equine connective tissue tumors of unknown etiology and a bovine papilloma virus (BPV)-induced equine tumor contained BPV-specific DNA sequences as determined by DNA-DNA hybridization of DNA from tumors with BPV DNA labeled in vitro. Analysis of the reassociation kinetics indicated that 20%-75% of the BPV genome was present in the various tumors. The number of partial BPV genome equivalents ranged from 60 to 500 copies per diploid quantity of cellular DNA. Thermal denaturation profiles of duplexes formed between labeled BPV DNA and DNA from tumor cells indicated that two tumors contained viral DNA with base sequences identical to BPV DNA. Three tumors (including DNA from the BPV-induced tumor) contained BPV-related DNA sequences that were less thermally stable. The decrease in thermal denaturation temperature may be due to the presence of (adenine + thymine)-rich regions of the BPV genome in the tumor cells. (38 refs.)

77-3877 **Chromatin-like Structures Obtained after Alkaline Disruption of Bovine and Human Papillomaviruses.** (Eng.) Favre, M. (Unite de Biochimie Enzymologie, Laboratoire de Pharmacologie Moleculaire, no. 147 Associe au Centre National de la Recherche Scientifique, Institut Gustav-Roussy, 94800 Villejuif, France) Breitburd, F.; Croissant, O.; Orth, G. *J Virol* 21(3): 1205-1209; 1977.

Four low-molecular-wt polypeptides with migrating properties similar to those of the calf liver histones H2a, H2b, H3, and H4 were detected by sodium dodecyl sulfate-polyacrylamide gel electrophoresis of highly purified preparations of bovine papilloma virus (BPV) and human papilloma virus (HPV). Complexes of these polypeptides and viral DNA were isolated by agarose gel filtration of the alkaline disruption products of both viruses. Under the electron microscope, these complexes appeared as circular structures composed of nucleosomes with a diameter of about 8 nanometers interconnected by a naked DNA filament. The max frequency of nucleosomes per molecule was 30 for both viruses, corresponding to a condensation ratio of the viral DNA of 2.5. (13 refs.)

77-3878 **Human Papillomavirus DNA: Physical Mapping of the Cleavage Sites of *Bacillus amyloliquefaciens* (*BamI*) and *Haemophilus parainfluenzae* (*Hpa*II) Endonucleases and Evidence for Partial Heterogeneity.** (Eng.) Favre, M. (Unite de Biochimie Enzymologie, Laboratoire de Pharmacologie Moleculaire, no. 147 Associe au Centre National de la Recherche Scientifique, Institut Gustave-Roussy, 94800 Villejuif, France) Orth, G.; Croissant, O.; Yaniv, M. *J Virol* 21(3): 1210-1214; 1977.

The DNA of human papillomavirus (HPV) obtained from a pool of plantar warts is cleaved by *Bacillus amyloliquefaciens* (*Bam*I) and *Haemophilus parainfluenzae* (*Hpa*II) restriction endonucleases at one and four specific sites, respectively. These sites were localized on the previously established cleavage map of HPV DNA, using the *Hin*d, *Hin*dIII, *Hpa*I, and *EcoR*I endonuclease restriction sites as reference. The four *HpaII* sites were mapped, clockwise, at 1.4%, 41.1%, 44.3%, and 52.8% of the genome length from the unique *Bam*I cleavage site taken as point zero. The *Hpa*II site mapped at 1.4% of the genome length was absent in 40% to 50% of the molecules, which demonstrates a genetic heterogeneity of HPV-DNA. (13 refs.)

77-3879 **Expression of Antigenic Crossreactivity to RD114 p30 Protein in a Human Fibrosarcoma Cell Line.** (Eng.) Smith, H. S. (Cell Culture Lab., Sch. Public Health, Univ. California at Berkeley, Berkeley, CA 94720) Riggs, J. L.; Springer, E. L. *Proc Natl Acad Sci USA* 74(2): 744-748; 1977.

An antigen with the 30,000-molecular wt protein (p30) of the feline endogenous oncornavirus RD114 was detected in a well-characterized human fibrosarcoma cell line, HT1080, by indirect immunofluorescence. Three antisera against RD114 p30 gave similar positive results, but two antisera against simian sarcoma virus p30, one antiserum against murine leukemia virus p30, and one antiserum against feline leukemia virus p30 gave no immunofluorescence. The reactivity observed with the RD114 p30 antiserum was detected in 10%-40% of the cells at early passages and was no longer expressed by the 41st subculture. The reactivity could be removed by adsorption of the antiserum with RD114-infected dog or human cells, but not by uninfected cells or by cells infected with an antigenically unrelated oncornavirus, feline leukemia virus. Neither complete virus particles nor reverse transcriptase (RNA-dependent DNA nucleotidyltransferase) activity was detected in the culture. These experiments suggest that the fibrosarcoma cell line expresses an antigen related to the p30 protein of the RD114 baboon endogenous virus group of oncornaviruses without producing complete virions. (40 refs.)

77-3880 **Gene Expression of Adenovirus Type 2: R-Loop Mapping of mRNA and Time Course of Viral DNA, mRNA, and Protein Synthesis.** (Eng.) Neuwald, P. D. (Biological Markers Program, Frederick Cancer Res. Center, P. O. Box B, Frederick, MD 21701) Meyer, J.; Maizel, J. V.; Westphal, H. *J Virol* 21(3): 1019-1030; 1977.

Adenovirus type 2 DNA was hybridized to early messenger RNA (mRNA) isolated from the cytoplasm of infected KB cells prior to the initiation of viral DNA synthesis. Resulting R loops were visualized in an electron microscope, and their positions were oriented with the help of DNA fragments generated by digestion with the restriction endonuclease *Bam* HI. Early RNA was found to map (in order of relative R-loop frequency) with midpoints near positions 0.95, 0.80, 0.03, 0.65, and 0.09 on the conventional adenovirus map. The time of appearance of individual viral mRNA's was compared with the time course of viral protein and DNA synthesis. A refined map of adenovirus gene function, based on these results and other available data, is presented. (46 refs.)

77-3881 **Electron Microscopy of Late Adenovirus Type 2 mRNA Hybridized to Double-stranded Viral DNA.** (Eng.) Meyer, J. (Biozentrum der Universitat Basel, Abteilung Mikrobiologie, CH-4056, Basel, Switzerland) Neuwald, P. D.; Lai, S. P.; Maizel, J. V.; Westphal, H. *J Virol* 21(3): 1010-1018; 1977.

R loops generated with late adenovirus type 2 (Ad2) messenger RNA (mRNA) in double-stranded viral DNA were visualized by electron microscopy. Unpaired DNA sequences in Ad2:Ad2+ND$_4$ heteroduplex DNA served as a visual marker for the orientation of R loops with respect to the conventional DNA map. The most abundant classes of late Ad2 mRNA hybridized, in order of R-loop frequency, with midpoints near positions 0.57, 0.88, 0.77, and 0.40 to 0.50 of the DNA map. The R loop at position 0.57 corresponded to a region containing the hexon gene; the one at position 0.88 corresponded to a region containing the fiber gene. The relative frequencies of these two R loops paralleled those of the encoded gene products. The mRNA sizes, calculated from those of the respective R loops, were slightly larger than those needed to code for these polypeptides. With use of the R-loop technique, two locations at which adjacent mRNA's hybridized to different strands were accurately mapped at positions 0.61 and 0.91 of the DNA. The map positions of late Ad2 mRNA correlated well with published RNA and protein maps. (39 refs.)

77-3882 **Purification and Characterization of the Phosphorylated DNA-binding Protein from Adenovirus-Type-2-infected Cells.** (Eng.) Linne, T. (Mikrobiologiska Institutionen, Biomedicinska Centrum, Box 581, S-75123 Uppsala, Sweden) Jornvall, H.; Philipson, L. *Eur J Biochem* 76(2): 481-490; 1977.

The virus-coded 72,000-molecular wt (MW) DNA-binding protein from HeLa cells infected with adenovirus type 3 was purified to homogeneity by DEAE-cellulose chromatography, selective precipitation, and gel filtration. This DNA-binding protein is phosphorylated, and the phosphate is covalently linked predominantly to serine. Analysis of tryptic digests of the ^{32}P-labeled 72,000-MW protein showed that the phosphate residue(s) is present in only one peptide. The DNA-binding fraction contains an additional nonphosphorylated protein with an approx MW of 45,000. Tryptic peptide maps of ^{35}S-methionine-labeled 72,000- and 45,000-MW polypeptides are indistinguishable. The amino acid compositions of the two polypeptides show closely related distributions. An antiserum produced against the purified 72,000-MW protein precipitates both the 72,000- and 45,000-MW proteins from extracts of adenovirus-infected cells. Immunofluorescence studies showed that the DNA-binding protein accumulated in characteristic structures in the nuclei of infected cells. (33 refs.)

77-3883 **Isolation of a Variant of Human Adenovirus Serotype 2 That Multiplies Efficiently on Monkey Cells.** (Eng.) Klessig, D. F. (Cold Spring Harbor Lab., Cold Spring Harbor, NY 11724) *J Virol* 21(3): 1241-1246; 1977.

A new variant of adenovirus serotype 2 (Ad2) that is able to multiply efficiently in monkey cells without the aid of simian virus 40 (SV40) is described. This variant overcomes the block to multiplication of wild-type Ad2 on monkey cells. The variant was selected, after nitrous acid mutagenesis, by sequential passage on monkey cells. This variant forms plaques with similar efficiency on human and monkey cells. Its growth kinetics and its burst size on human and monkey cells are similar. These growth properties are similar to those found for wild-type Ad2 on monkey cells when the block is overcome by coinfection with SV40. (15 refs.)

77-3884 **In Vivo and In Vitro Phosphorylation of the Adenovirus Type 5 Single-Strand-specific DNA-binding Protein.** (Eng.) Levinson, A. D. (Dept. Biochemical Sciences, Princeton Univ., Princeton, NJ 08540) Postel, E. H.; Levine, A. J. *Virology* 79(1): 144-159; 1977.

Evidence is presented that the 72,000-molecular wt (MW), single-strand-specific DNA-binding protein of adenovirus type 5 can be labeled with $^{32}PO_4$ added as inorganic phosphate to the medium of infected monkey or human kidney cells. The DNA-binding protein in the infected cell can be isolated as a phosphoprotein at early and late times after infection. Most or all of the ^{32}P-phosphate can be removed from the DNA-binding protein by alkaline phosphatase or hydrolysis at alkaline pH. The dephosphorylated protein retains the ability to bind specifically to single-stranded DNA. Cells infected with the H5ts125 temperature-sensitive mutants of adenovirus type 5, which contains a mutation in the structural gene of the 72,000-MW protein, failed to phosphorylate this protein at the nonpermissive temperature, even though they synthesized approx normal (wild-type) levels of the protein during short labeling times (30 min). An in vitro nuclear protein kinase assay is described that can detect the phosphorylation of three adenovirus-induced phosphoproteins (100,000, 72,000, 36,000 MW) that are also observed when adenovirus-infected cells are labeled with inorganic ^{32}P-phosphate in vivo. The protein kinase activity detected in this in vitro assay is not dependent on or stimulated by the addition of exogenous cyclic AMP or cyclic guanosine monophosphate. The 72,000-MW protein phosphorylated in vitro by this phosphokinase activity has been shown to be the adenovirus single-strand-specific DNA-binding protein by a specific immunoprecipitation test. (24 refs.)

77-3885 **Characterization of a Temperature-sensitive Mutant of Human Adenovirus Type 7.** (Eng.) Estes, M. K. (Dept. Virology and Epidemiology, Baylor Coll. Medicine, Houston, TX 77030) Butel, J. S. *J Virol* 21(3): 1159-1169; 1977.

The properties of a naturally occurring temperature-sensitive (ts) mutant of human adenovirus type 7 (Ad7) were studied. Mutant Ad7 (19), or E46-, was the nonhybrid adenovirus component derived from a defective simian virus 40 (SV40)-Ad7 hybrid (PARA). The growth of the mutant was restricted at 40.5 C, and the ratios of virus yields in KB cells at 40.5 and 33 C were 10^{-2} to 10^{-3}. Viral DNA synthesis and the synthesis of adenovirus-specific antigens (tumor, capsid, hexon, and penton antigens) appeared normal at the restrictive temperature. The assembly of virus particles was aberrant, as determined by thin section of the infected cells. The infectivity of mutant virions was heat-labile at 50 C, suggesting a ts defect in a structural component of the virion. Polyacrylamide gel electrophoresis (PAGE) of ^{35}S-methionine-labeled polypeptides synthesized in mutant-infected cells suggested that at least the major virion polypeptides were synthesized at the restrictive temperature. A lack of inhibition of host protein synthesis late in mutant infections, compared with wild-type (WT) infections at both the permissive and nonpermissive temperature, made quantitation of infected-cell polypeptides difficult. Analysis of the assembly of capsomeres from cytoplasmic extracts of infected cells on sucrose gradients and by nondissociating PAGE suggested that hexon capsomeres were made at 40.5 C. The hexon capsomeres synthesized by the mutant at either 33 or 40.5 C displayed a decreased migration in the nondissociating gel compared with the WT hexon capsomeres. The molecular wt of the mutant and WT hexon polypeptides were identical. These results suggest that the ts lesion of this group B human Ad7 mutant may be reflected in altered hexons. The mutant Ad7 interfered with the replication of Ad2 and Ad21 at the elevated temperature. (43 refs.)

77-3886 **Changes in Isoenzyme Spectra Associated with Energy Metabolism as an Index of Rearrangement in Cell Genome Expression During Transformation by an Oncogenic Virus.** (Rus.) Ageenko, A. I. (P. A. Gertsen Moscow Oncological Inst., Moscow, USSR) Vitorgan, Iu. E.; Gorozhanskaia, E. G. *Vestn Akad Med Nauk SSSR* (3): 19-22; 1977.

Changes in the isoenzyme spectra and activities of hexokinase (HK), lactate dehydrogenase (LDH), and malate dehydrogenase (MDH) were studied in rat embryo fibroblasts (REF) inoculated with oncogenic adenovirus Ad12 and infectious adenovirus Ad6. Infection with Ad6 did not change HK activity, but it did alter the spectrum of LDH. However, nuclear HK activity in the REF inoculated with Ad12 was significantly elevated: the activity started to increase on day 3 after infection, and on day 24 it was three to five times higher than that in control cells. Cytoplasmic HK activity started to increase on day 5 after infection; this activity was 6.6 times higher than that in controls on day 18 and almost 14 times higher on day 24. Ad12 reduced cytoplasmic LDH-3 activity and elevated nuclear LDH-1 activity; nuclear MDH-1 activity was significantly increased on days 5 and 18, cytoplasmic MDH-3 activity on days 3 and 24. (7 refs.)

77-3887 **Initiation and Termination Sites of Adenovirus 12 DNA Replication.** (Eng.) Ariga, H. (Dept. Tumor Virus Res., Inst. Medical Science, Univ. Tokyo, 4-6-1, Shirokane-dai, Minato-ku, Tokyo 108, Japan) Shimojo, H. *Virology* 78(2): 415-424; 1977.

The initiation and termination sites of adenovirus 12 (Ad12) DNA replication were determined using temperature-sensitive (ts) mutants that were defective in the initiation of DNA replication at a restrictive temperature. Secondary cultures of human embryo kidney cells and monolayer cultures of KB cells were used. Thirty hours after infection with ts Ad12, the cells were pulse-labeled with ^{3}H-thymidine for 5 min, and viral DNA molecules labeled at either the initiation or termination sites were isolated and cleaved with a restriction endonuclease (Eco RI or Bam HI). The highest radioactivities were found at both ends of DNA, indicating that the initiation and termination sites are located at or near both ends of the genome. The change in the proportion of ^{3}H-labeled replicating DNA to uniformly labeled DNA was determined at various times after the shift down to a permissive temperature. The pattern of labeling suggests that Ad12 DNA replication initiates at or near each end of the genome and proceeds bidirectionally to the opposite end. (20 refs.)

77-3888 **Morphogenesis of Poliovirus. IV. Existence of Particles Sedimenting at 150S and Having the Properties of Provirion.** (Eng.) Guttman, N. (Dept. Virology, Hebrew Univ., Hadassah Medical Sch., Jerusalem, Israel) Baltimore, D. *J Virol* 23(2): 363-367; 1977.

A particle that sediments at 150S and has properties associated with the provirion to poliovirus has been isolated from HeLa cells infected with Mahoney type 1 poliovirus. After it binds to cells, this precursor can be eluted and sedimented at 125S. (13 refs.)

77-3889 **Encephalomyocarditis Virus RNA. II. Polyadenylic Acid Requirement for Efficient Translation.** (Eng.) Hruby, D. E. (Dept. Microbiology and Immunology, Univ. Colorado Medical Center, Denver, CO 80262) Roberts, W. K. *J Virol* 23(2): 338-344; 1977.

The role of polyadenylic acid (poly A) in the replication of encephalomyocarditis virus was investigated in cell-free extracts from Ehrlich ascites tumor cells. The presence of poly A stimulated the overall translation of the virus two- to three-fold. This finding is in contrast to those of, previous studies, possibly as a result of the use of different techniques. (27 refs.)

77-3890 **More Hydatidiform Moles (Letter to Editor)?** (Eng.) Barr, S. J. (Fazakerley Hosp., Liverpool, England) *Br Med J* 2(6088): 707-708; 1977.

Of 13 hydatidiform mole patients, all had had influenza at or around the time of conception; in 6 cases, the husband also was a victim of the virus. Viral infection early in pregnancy may be associated with fetal abnormalities. (no refs.)

77-3891 Electronmicroscopic Observation of the Virus in Cells Obtained from a Sputum Cytology. (Eng.) Frable, W. J. (Box 115, Medical Coll. Virginia, Richmond, VA 23298) Kay, S. *Acta Cytol (Baltimore)* 21(3): 391-393; 1977.

Cytological examination of the sputum samples of a 64-yr-old man who was thought to have pneumonia revealed that he had a herpesvirus infection of the respiratory tract. Routine Papanicolaou-stained slides showed the presence of cell changes typical of herpesvirus infection. Electron photomicrographs demonstrated numerous viral particles in several cells. The av diameter of the particles was 100 nanometers, and particles with and without a central core were observed. The particles were concentrated in the center of the nuclei, with displacement of the nuclear chromatin. The blending technique of Saccomanno plus the addition of standard methodology for electron-microscopic specimens proved satisfactory for revealing the ultrastructural details of the virus. (10 refs.)

77-3892 **Biochemical Evidence for Viral-like Characteristics in Cerebrospinal Fluid of Brain Tumor Patients.** (Eng.) Cuatico, W. (Post Office Box 1666, Idaho Falls, ID 83401) Woldron, R.; Tyschenko, W. *Cancer* 39(5): 2240-2246; 1977.

Cerebrospinal fluid (CSF) from 15 patients with various types of CNS tumors and from 5 patients with unrelated diseases was analyzed for the presence of core and subcore fragments of virallike particles and for the ability of the core fraction to make DNA from deoxynucleotide precursors. The hybridization of this DNA to the polysomal RNA of solid glioblastoma was also studied. Of the 15 CSF samples from the tumor patients, 10 demonstrated the presence of core fragments, 8 lemonstrated the presence of subcore fragments, and the core ractions of 11 samples synthesized detectable amounts of DNA. Four of the samples were negative for all three parameters. None of the control CSF samples were positive for any of the parameters. The DNA synthesized from particles in he CSF of a medulloblastoma patient hybridized to cytoplasnic RNA derived from a glioblastoma, but not to similar RNA from normal brain tissue. It is concluded that CNS umor tissue sheds particles similar in properties to RNA umor viruses into the CSF. (10 refs.)

77-3893 **Oncornavirus Markers on Peripheral Lymphocytes of Breast Cancer Patients (Meeting Abstract).** (Eng.) Wiseman, C. (M.D. Anderson Hosp. and Tumor Inst., Houston, TX 77030) Bowen, J.; Robinson, B.; Blumenschein, G. *Proc Am Assoc Cancer Res* 18: 172; 1977. (no refs.)

77-3894 **Purification and Characterization of the DNA Polymerase of Human Breast Cancer Particles.** (Eng.) Ohno, T. (Inst. Cancer Res., Coll. Physicians and Surgeons Columbia Univ., 701 W. 168 St., New York, NY 10032) Sweet, R. W.; Hu, R.; Dejak, D.; Spiegelman, S. *Proc Natl Acad Sci USA* 74(2): 764-768; 1977.

The purification and characterization of an RNA-dependent DNA polymerase from human breast cancer particles are reported. Its key properties are similar to those of the reverse transcriptases found in murine mammary tumor virus and Mason-Pfizer monkey virus. Like these viral enzymes, the human breast cancer enzyme exhibits the following properties that distinguish the known viral reverse transcriptases from normal cellular DNA polymerases: (1) a strong preference for oligo(dT)-poly(rA) over oligo(dT)-poly(dA) as a template for the synthesis of poly(dT); (2) the acceptance of the highly specific oligo(dG)-poly(rCm) as a template for the formation of poly(dG); (3) the ability to use a viral RNA-(AMV) as a template to fashion a faithful DNA complementary copy; and (4) its preference for Mg^{++} over Mn^{++}. The data are further evidence of the similarities between the viruslike particles in human breast cancers and the viral agents associated with the corresponding malignancies in the mouse and monkey models. No enzyme with these properties has been detected in normal breast tissues or in benign breast tumors. (19 refs.)

77-3895 **Spontaneous and Induced Patterns of the Epstein-Barr Virus (EBV) Cycle in a New Set of Somatic Cell Hybrids.** (Eng.) Klein, G. (Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden) Clements, G.; Zeuthen, J.; Westman, A. *Cancer Lett* 3(1/2): 91-98; 1977.

A somatic cell hybrid line and its subclones obtained by fusing two Burkitt's lymphoma lines (Raji and Namalwa) were examined for the expression of Epstein-Barr virus (EBV)-specific antigens, both spontaneously and after induction. The hybrids retained spontaneous early antigen (EA) production at the level characteristic of Raji. Similarly, the more permissive Raji pattern dominated the induction of EA by 5-iodo-2-deoxyuridine treatment or R_3HR-1 virus superinfection. These findings agree with previous results on independently derived Raji/Namalwa hybrids. Virus capsid antigen was induced in the hybrids by P^3HR-1 virus superinfection, though at a lower level than in the Raji parental cell. (18 refs.)

77-3896 **Early Acquisition of Cytomegalovirus and Epstein-Barr Virus Antibody in Several Isolated Melanesian Populations.** (Eng.) Lang, D. J. (Dept. Pediatrics, Box 2920, Duke Univ. Medical Center, Durham, NC 27710) Garruto, R. M.; Gajdusek, D. C. *Am J Epidemiol* 105(5): 480-487; 1977.

There are significant differences among diverse human populations in the seroepidemiology of cytomegalovirus (CMV) and Epstein-Barr virus (EBV). A very high rate of early acquisition of antibody to CMV and EBV was found among three remote populations living in the Eastern Highlands of Papua New Guinea, the Solomon Islands, and the New Hebrides, respectively. These three genetically distinct populations, living in widely different ecologies and social settings, each had the same pattern of early acquisition of infection with both viruses. It is suggested that the spread of CMV and EBV is determined by patterns of interpersonal contact as well as by the prevalence of virus-shedders. The large number of handlers of each infant in these studied groups appears directly related to the early acquisition of these viruses. (35 refs.)

77-3897 **Studies of a Herpesvirus Isolated from a Cell Line Derived from Kaposi's Sarcoma (Meeting Abstract).** (Eng.) Glaser, R. (Pennsylvania State Univ. Coll. Medicine, Hershey, PA 17033) Geder, L. *Proc Am Assoc Cancer Res* 18: 30; 1977. (no refs.)

77-3898 **Photodynamic Inactivation of Herpes Simplex Virus and Its DNA.** (Eng.) Melnick, J. L. (Dept. Virology and Epidemiology, Baylor Coll. Medicine, Houston, TX 77030) Khan, N. C.; Biswal, N. *Photochem Photobiol* 25(4): 341-342; 1977.

Light with a wavelength of 450 nanometers has been found to be most effective in destroying proflavine-sensitized herpes simplex virus (HSV) so that it could no longer infect or transform cells. DNA isolated from HSV or HSV-infected cells (with specific infectivity of 1,500 and 1,800 plaque-forming units/μg, respectively) rapidly and completely lost this infectivity when photodynamically inactivated. (19 refs.)

77-3899 **Influence of Dibutryl Cyclic AMP on Thymidine Uptake by Herpes Simplex Virus Infected Cells and the Intracellular Level of Cyclic AMP.** (Eng.) Bittlingmaier, K. (Div. Experimental Virology, Inst. Medical Microbiology, Johannes Gutenberg Univ., D-6500 Mainz, W. Germany) Schneider, D.; Falke, D. *Biochim Biophys Acta* 477(3): 228-238; 1977.

The effect of dibutryl cyclic AMP (Bt_2-cAMP) on deoxythymidine (dThd) transport and other virus-induced processes was studied in baby hamster kidney (BHK-21) cells and primary rabbit kidney cells infected with herpesvirus hominis, types 1 and 2. Bt_2-cAMP inhibited the increase of dThd and bromodeoxyuridine transport normally observed after infection with both viruses. Incorporation was also reduced. Inhibition of uptake was noncompetitive, as analyzed by the Lineweaver-Burk plot. Addition of the drug to infected cells also reduced the activity of thymidine kinase. Transport of deoxyuridine, deoxycytidine, and deoxyadenosine was not reduced. At 4-8 hr after infection with thymidine kinase (+) herpes strains, the level of cAMP increased. On infection with a thymidine kinase (-) virus, only a small elevation of cAMP occurred. Early addition of actinomycin D or cycloheximide prevented the increase in cAMP. This increase seems to depend on the activity of the herpes genome, because UV irradiation of infective particles destroys this effect. (27 refs.)

77-3900 **Quantitation of Herpes Simplex Virus Type 1 RNA in Infected HeLa Cells.** (Eng.) Stringer, J. R. (Dept. Molecular Biology and Biochemistry, Univ. California, Irvine, CA 92664) Holland, L. E.; Swanstrom, R. I.; Pivo, K.; Wagner, E. K. *J Virol* 21(3): 889-901; 1977.

The size and the amount of herpes simplex virus (HSV)-specific RNA synthesized in HeLa cells were quantitated by DNA and RNA excess hybridization. At 2 hr after infection (early), transcripts from 20% of the total HSV DNA are present on polyribosomes as poly(A+) RNA. At this time, viral poly(A+) RNA comprises 60%-75% of the newly synthesized poly(A+) messenger RNA (mRNA) on polyribosomes. By 6 hr (late), poly(A+) HSV RNA transcribed from 35% to 40% of the viral DNA is found on polyribosomes. These viral poly(A+) transcripts comprise as much as 90% of newly synthesized poly(A+) mRNA and are measurably larger than viral poly(A+) transcripts isolated early. Some but not all of this size difference is due to the fact that the poly(A) tails on early transcripts are shorter than those on late transcripts. Even late after infection, a small but readily measurable amount of cellular poly(A+) RNA is still being synthesized and is entering polyribosome complexes. In the nucleus, late after infection, poly(A+) HSV RNA is complementary to 50% of the total HSV DNA. Both early and late after infection, the total nuclear viral transcripts are larger than the viral transcripts on polyribosomes; however, nuclear HSV poly(A+) RNA is not measurably larger than the corresponding cytoplasmic viral poly(A+) sequences at either time. A major portion (30%-40%) of the polyribosomal HSV RNA synthesized either early or late after infection is not polyadenylated. This HSV poly(A-) RNA is transcribed from the same sequences as HSV poly(A+) RNA but, when labeled and isolated either early or late after infection, both nuclear and polyribosomal viral poly(A-) RNA molecules sediment faster in sucrose-formaldehyde gradients than their polyadenylated counterparts. (28 refs.)

77-3901 **Evidence That Herpes Simplex Virus DNA Is Transcribed by Cellular RNA Polymerase B.** (Eng.) Costanzo, F. (Istituto di Microbiologia e Virologia, Universita di Bologna, Bologna, Italy) Campadelli-Fiume, G.; Foa-Tomasi, L.; Cassai, E. *J Virol* 21(3): 996-1001; 1977.

Amanitin is a toxin that allows division of nuclear eukaryotic RNA polymerases into two categories: amanitin insensitive (RNA polymerase I and amanitin-sensitive (RNA polymerase II). In herpes simplex virus type 1 (HSV-1)-infected HEp-2 cells, amanitin added before or at various times after infection reduced viral multiplication. Also, the three waves of transcription of HSV-1 DNA, which lead to the synthesis of α, β-, and γ-polypeptides, were all sensitive to amanitin in HEp-2 cells, and the amanitin-sensitive RNA polymerase activities of isolated nuclei were equally sensitive to the inhibitor before and during infection. In contrast, HSV-1 DNA transcription was totally unaffected by amanitin in AR1/9-5B cells, a mutant subline of Chinese hamster ovary cells that possesses an amanitin-resistant RNA polymerase B. Together, these results strongly suggest that HSV-1 DNA utilizes for its transcription a polymerase indistinguishable from host cell RNA polymerase B with respect to sensitivity to amanitin. (22 refs.)

77-3902 **Cytogenetic Study of Human Lymphocyte Cultures Infected with Herpes Simplex Virus Strains.** (Bul.) Mincheva, A. (Medical Acad., Res. Inst. Infectious and Parasitic Diseases, Bulgaria) Dundarov, S.; Manolov, G. *Onkologiia* 13(4): 169-171; 1976.

The effect of herpes simplex viruses (HSV) of different serotype on the chromosomes of human WBC was studied. The WBC were cultivated for 72 hr; the cultures were infected after 68 hr with DP and TM (type 1), DD_3 and BJ (type 2), and MB_1 (intermediate) strains of HSV. The multiplicity of infection was $M = 0.75$. To ascertain the effect of the strains, 100-300 disconnected metaphases were analyzed. There were breaks and gaps in the structure of the chromatids and isochromatids 4 hr after infection. Group A chromosomes were affected equally by HSV types 1 and 2: repeatedly damaged segments were observed in chromosomes 1 and 3, as well as in those from the unidentified Groups B, C, and D. (6 refs.)

77-3903 **Role of Oncornaviruses in Carcinoma of the Prostate.** (Eng.) McCombs, R. M. (Post Office Box 1980, Eastern Virginia Medical Sch., Norfolk, VA 23501) *Cancer Treat Rep* 61(2): 131-132; 1977.

The existence of oncornavirus genetic information in human prostatic tissue was studied by assaying for products of viral gene expression (ie, the p30 antigen). Tissue samples from patients wtih benign prostatic hyperplasia (BPH) or prostatic carcinoma (CaP) were assayed by competitive radioimmunoassay. The competing antigens used were p30 proteins derived from simian sarcoma virus type 1 (SSV-1) and Rauscher murine leukemia virus (RLV). Three of 20 extracts from BPH patients and 1/20 from CaP patients competed with the SSV-1 p30 antigen; none of 10 extracts from CaP patients and only 1/10 extracts from BPH patients competed with the RLV p30 antigen. The significance of these findings was not established. (6 refs.)

77-3904 **Isolation of a Herpesvirus from the Cell Culture of a Malignant Melanoma of a Ground Squirrel (*Spermophilus tridecemlineatus*).** (Eng.) Dutta, S. K. (Dept. Veterinary Science, Univ. Maryland, College Park, MD 20742) Gorgacz, E. J.; Albert, T. F.; Ingling, A. L. *Am J Vet Res* 38(5): 591-595; 1977.

An sc neoplastic mass in a 13-lined ground squirrel that metastasized to the regional lymph nodes and lung was studied. Histopathologically, the tumor architecture and cellular morphology were compatible with a malignant amelanotic melanoma. Ultrastructurally, the neoplastic tissue was composed of oval cells, spindle-shaped cells, and spindle-shaped cells with electron-dense cytoplasmic granules. Virus particles were not seen in these cells. Cell cultures of the neoplastic tissue grew in complete monolayers and, on initial passages, contained a few herpesvirus particles. Secondary monolayer cell cultures, when exposed to 5-iodo-2′-deoxyuridine or made into several serial subculture passages, showed cytopathic effects and contained many virus particles. The ground squirrel virus contained DNA, was sensitive to chloroform treatment, and had herpesvirus characteristics upon electron microscopy. The buoyant density of the virus was 1.298 g/cm^3, and the diameter of the enveloped virus particles was 146 nanometers. This ground squirrel herpesvirus was antigenically distinct from other known herpesviruses. (20 refs.)

77-3905 ***Herpesvirus saimiri*-induced Lymphoproliferative Disease in Howler Monkeys.** (Eng.) Rangan, S. R. (Tulane Univ., Delta Regional Primate Res. Center, Covington, LA 70433) Martin, L. N.; Enright, F. M.; Abee, C. R. *J Natl Cancer Inst* 59(1): 165-171; 1977.

Four of five howler monkeys (*Alouatta caraya*) experimentally infected with *Herpesvirus saimiri* (HVS, $10^{5.2}$ median tissue culture infective dose) developed a rapidly fatal malignant lymphoma accompanied by peripheral T-cell lymphocytosis. HVS was isolated from fresh and tissue-cultured blood and tissue lymphocytes and from cell cultures derived from nonlymphoid organs. Humoral antibodies against HVS-induced antigens were detected in the sera of the animals. The in vitro response of the peripheral blood lymphocytes to mitogenic stimulants was depressed following HVS infection. (28 refs.)

77-3906 **Infectious Human and Non-Human Primate RNA Tumor Virus Proviral DNA in Productively Infected Cells (Meeting Abstract).** (Eng.) Markham, P. D. (Litton Bionetics, Inc. and NCI, Bethesda, MD 20014) Gallo, R. C.; Sarin, P. *Proc Am Assoc Cancer Res* 18: 230; 1977. (no refs.)

77-3907 **Divergence of Baboon Endogenous Type C Virogenes in Primates: Genomic Viral RNA in Molecular Hybridization Experiments.** (Eng.) Donehower, L. (Lab. Tumor Cell Biology, NCI, Bethesda, MD 20014) Wong-Staal, F.; Gillespie, D. *J Virol* 21(3): 932-941; 1977.

The RNA genome of an endogenous C-type RNA virus from a baboon (BaEV) was used to measure the divergence of BaEV-related virogenes among primates, to compare these results with those of experiments using complementary DNA from BaEV. RNA purified from two related RNA tumor viruses, one isolated from a baboon, *Papio anubis*, and the second from cultured blood WBC of a patient with acute myelogenous leukemia, was labeled with ^{125}I and hybridized to DNA from different primates. RNA from both viruses showed max sequence homology with genes of baboons and little homology with genes of humans. The results confirm earlier suggestions that both viruses originated by transcription of baboon virogenes and that one was transmitted to humans in nature. Hybridization of the viral RNA to cell DNA followed complicated kinetic patterns, indicating the presence of both repeated and infrequent virogene elements. This conclusion was verified in experiments using varied DNA:RNA ratios. It is proposed that virogenes, although composed of genes repeated 10 times or more, consist of some sequences more preferentially conserved than others. The nonuniformity of virogene sequence conservation limits the use of viral probes in studies of certain aspects of virogene evolution. (28 refs.)

77-3908 **Host-determined Differences in Expression of Surface Marker Characteristics on Human and Simian Lymphoblastoid Cell Lines Transformed by Epstein-Barr Virus.** (Eng.) Robinson, J. E. (Dept. Pediatrics, Yale Univ. Sch. Medicine, New Haven, CT 06510) Andiman, W. A.; Henderson, E.; Miller, G. *Proc Natl Acad Sci USA* 74(2): 749-753; 1977.

Differences in the biologic behavior of Epstein-Barr virus in different primate species were examined by studying lymphocyte surface markers on primary and transformed cells of three species. Among primary WBC, the distribution of cells with characteristics of B cells was similar in humans, woolly monkeys, and cotton-top marmosets. However, after transformation by Epstein-Barr virus, cells from each species were characteristically different. Transformed human umbilical cord cells expressed the complement receptor, monkey cells exhibited both this receptor and the receptor for IgG Fc (EA7S), and marmoset cells did not have either surface marker. In both human and marmoset WBC, the highest efficiencies of transformation were found in subpopulations with the greatest numbers of cells with the receptor. The data suggest that in all species, a cell with the complement receptor is susceptible to transformation; however, this receptor is not expressed on transformed marmoset cells. Thus, it is necessary to distinguish between Epstein-Barr virus-induced transformation of growth properties (immortalization) and transformation of cell surface properties. (20 refs.)

77-3909 **Characterization of Lymphoid Cell Lines Established from Multiple Epstein-Barr Virus (EBV)-induced Lymphomas in a Cotton-topped Marmoset.** (Eng.) Rabin, H. (Viral Oncology Program, NCI, Frederick Cancer Res. Center, Post Office Box B, Frederick, MD 21701) Neubauer, R. H.; Hopkins, R. F.; Levy, B. M. *Int J Cancer* 20(1): 44-50; 1977.

A cotton-topped marmoset inoculated with cell-free Epstein-Barr virus (EBV), strain B95-8, developed lymphomas in liver, spleen and mesenteric lymph nodes. Continuous suspension cell lines were established from tumor tissue from each of these three sites. Cells of each line were positive for intracellular EBV antigens and EB nuclear antigen and they released low levels of transforming virus. Soon after initial culturing each line had a high frequency of cells (84%-85%) with receptors for activated complement, but these receptors were no longer evident on retesting several mo later. All three lines initially showed high levels of cells that stained for surface λ light chain and α and μ heavy chains. Cells of all three lines showed a decrease in γ chain staining, and the lymph-node tumor line showed reductions in surface staining for μ and λ chains as well after prolonged cultivation. Clonal cells of the three lines resembled their respective parental lines in surface markers. Cytogenetically, all the lines were hypodiploid, $2n = 45$, and several karyotypes from all three lines showed the loss of a medium-sized metacentric chromosome. A marker chromosome with an extra band in the centromeric region was apparent in the lymph-node tumor line. Because the three tumors were similar in many ways, it is possible that they had a common cell origin, as is the case with Burkitt's lymphoma in humans. (17 refs.)

77-3910 **Establishment of Simian Sarcoma Virus, Type 1 (SSV-1)-transformed Non-producer Marmoset Cell Lines.** (Eng.) Bergholz, C. M. (Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612) Wolfe, L. G.; Deinhardt, F. *Int J Cancer* 20(1): 101-111; 1977.

Primate cell lines transformed by simian sarcoma virus, type 1 (SSV-1) were established in the absence of virus production to facilitate investigation of SSV gene functions, analysis of virus- vs tumor-specific antigens, and isolation of SSV-1 sarcoma-specific DNA. SSV-1 transformed nonproducer cell lines were established by infection of normal marmoset fibroblast cells (HF) with limiting dilutions of SSV-1. Four focus-derived cell lines were identified as nonproducers by assay of culture fluids for focus-forming activity and by the mixed culture cytopathogenicity test with XC cells. Further studies failed to detect C-type virus production by ^{3}H-uridine labeling, reverse-transcriptase assay, or electron microscopy The nonproducer cell lines, designated HF/SSV-NPI, IV, V and VI, appeared morphologically transformed and cloned in soft agar with the same efficiency as HF/SSV-1 virus-producing transformed cells. Expression of either cytoplasmic or cell surface virus-related antigens was not detected by immunofluorescence or serum cytotoxicity tests. The presence of sarcoma genome in the transformed nonproducer cell lines was demonstrated by rescue of focus-forming activity following superinfection with nontransforming helper virus or by cocultivation with helper-virus-producing cell lines. (31 refs.)

77-3911 **Oncogenicity in Marmosets of HL-23V, a Type C Oncornavirus Isolated from Human Leukemic Cells, and Comparison with Simian Sarcoma Virus Type 1 (SSV-1/SSAV-1).** (Eng.) Bergholz, C. M. (Dept. Microbiology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612) Wolfe, L. G.; Deinhardt, F.; Thakkar, B. Marczynska, B. *J Natl Cancer Inst* 58(4): 1041-1046; 1977

Following infection with HL-23V virus, which was isolated from the cultured WBC of an acute myelogenous leukemia patient, dog thymus cells (A7573) produced a C-type virus hat transformed marmoset and horse cells in vitro and inluced virus-producing fibromas in marmosets. The tumors ind transformed foci were indistinguishable morphologically rom those induced by simian sarcoma virus 1 (SSV-1/SSAV-l). HL-23V was indistinguishable from SSV-1/SSAV-1 by mmunofluorescence and neutralization tests, and the nonransforming virus associated with HL-23V completely inhibted SSV-1 focus induction in interference tests. Cell cultures stablished from a marmoset fibroma produced a transformng and nontransforming virus biologically and antigenically dentical to HL-23V and SSV-1/SSAV-1. (35 refs.)

77-3912 **Sulphated Acid Mucopolysaccharides in SV40-transformed Human Cells from Normal and Mucopolysaccharidosis Patients.** (Eng.) Webb, T. (Dept. Cancer Studies, Medical Sch., Univ. Birmingham, Birmingham B15 2TJ, England) *Br J Cancer* 36(1): 72-77; 1977.

SV40-transformed fibroblasts of normal individuals and patients suffering from one of the mucopolysaccharidoses or mucopolysaccharide-storage diseases have a reduced capacity to secrete sulfated acid mucopolysaccharides into the growth medium. Alterations in the stability of RNA species after transformation may lead to this altered enzymatic function. (25 refs.)

77-3913 **Response of Human Diploid Fibroblasts to Infection with Simian Virus 40 (Meeting Abstract).** (Eng.) Lehman, J. M. (Univ. Colorado Medical Center, Denver, CO 80262) Lehman, E.; Solomons, C. C. *Proc Am Assoc Cancer Res* 18: 68; 1977. (no refs.)

77-3914 **A Lack of Correlation Between "T" Antigen and Any Particular Human Chromosome in Hybrids Made Between SV40 Transformed Human Fibroblasts and Mouse LMTK- Cells.** (Eng.) Webb, T. (Dept. Cancer Studies, Univ. Birmingham, Medical Sch., Birmingham B15 2TJ, England) Harding, M. *Cancer Lett (Amsterdam)* 3(1/2): 15-21; 1977.

Fourteen lines of hybrid cells were established by fusion of mouse LMTK- (thymidine kinase-negative) cells with simian virus 40 (SV40) transformed human fibroblasts. The lines were examined for the presence of SV40 T antigen, and the human chromosomes they carried were identified by Giemsa banding. The cells retained high levels of chromosomes 4, 7, 11, 17, and 18, but there was no significant correlation between any particular chromosome and the presence of SV40 virus. (12 refs.)

77-3915 **Nucleotide Sequence of the Restriction Fragment Hind F-Eco RI2 of SV40 DNA.** (Eng.) Contreras, R. (Lab. Molecular Biology, Univ. Ghent, Ledeganckstraat, 35, 9000 Ghent, Belgium) Volckaert, G.; Thys, F.; Van de Voorde, A.; Fiers, W. *Nucleic Acids Res* 4(4): 1001-1014; 1977.

The nucleotide sequence of the simian virus 40 genome region between the Hind K fragment and the Eco RI cleavage site was determined by a combination of three different approaches: analysis of RNA products obtained by transcription with *Escherichia coli* DNA-dependent RNA polymerase, partial degradations with snake venome exonuclease, and base-specific chemical degradation of 5′-terminal-labeled restriction fragments. The nucleotide sequence shows only one open reading frame, permitting the deduction of a small segment of the amino acid sequence of VP_1, the major structural protein. (19 refs.)

77-3916 **Mapping of Transcription Sites of Simian Virus 40-specific Late 16S and 19S mRNA by Electron Microscopy.** (Eng.) May, E. (NIH, Bethesda, MD 20014) Maizel, J. V.; Salzman, N. P. *Proc Natl Acad Sci USA* 74(2): 496-500; 1977.

Simian virus 40 (SV40) late 19S and 16S messenger RNA's (mRNA's) were annealed to complementary regions of partially melted viral double-stranded SV40(L*Hpa* II) DNA or SV40(L*Bam* HI) DNA. The RNA.DNA hybrid regions within the DNA molecules were visualized as loops [with SV40(L*Hpa* II) DNA] or branched molecules [with SV40(L *Bam* HI) DNA] in the electron microscope. The data confirm the previous localizations of the 3′ and 5′ ends of 16S SV40 mRNA and of the 3′ end of late 19S SV40 mRNA. The 5′ end of the major stable SV40 late 19S mRNA has been positioned at 0.755 map unit. Thus, sequences of viral DNA from 0.655 to 0.755 map unit, including the replication origin, are not converted into major stable species of late viral mRNA. (29 refs.)

77-3917 **Nucleotide Sequence of the Restriction Fragments Hind L and Hind M of SV40 DNA.** (Eng.) Ysebaert, M. (Lab. Molecular Biology, Univ. Ghent, Ledeganckstraat 35, 9000 Ghent, Belgium) Thys, F.; Van de Voorde, A.; Fiers, W. *Nucleic Acids Res* 3(12): 3409-3421; 1976.

The nucleotide sequence of the restriction fragments Hind M and Hind L of simian virus 40 DNA was assessed. The labeling of approx 0.1 μg DNA fragment usually resulted in a radioactivity of 5-20 x 10^6 disintegrations/min, depending primarily on the purity of the fragment and the specific activity of the ^{32}P-ATP. Because of the significant difference in base composition between the two strands of Hind M and Hind

L, the strand separation presented no difficulties. Their nucleotide sequence was deduced by the wandering spot method; the information derived from the two strands was partly complementary. The chemical degradation method gave good results with double strands but was not satisfactory with the single strands from these small restriction fragments, even after removal of the RNA by alkaline degradation. However, strand separation could be performed after the modification reactions if extreme temperatures or values were avoided. Some loss of the DNA fragment and a high RNA concentration after strand separation were the drawbacks of this modification. By comparing the four nucleotide-specific lanes of each strand on the autoradiograph, the nucleotide sequences could be deduced. They agreed with the data from the wandering spot procedure. In the cytidine + thymidine lane, the spots due to degradation of a cytidine residue were more intense than those corresponding to degradation of a thymidine residue. The nucleotide sequence in the region near the 3′-end could not be determined because of the high RNA concentration in the samples derived from homochromatography. The sharpness of the polyacrylamide gel pattern could be increased by removing this RNA with a heat-treated mixture of deoxyribonuclease-free ribonuclease, followed by precipitation of the reaction mixture with ethanol. In the case of strand A from Hin L, the autoradiograph demonstrated that near the 3′-end, two or more thymidines were followed by two or more cytidines. Three spots for the thymidine lane and three spots for the cytidine lane were revealed. Identification of the 5′-terminal nucleotide of the separated strands showed that strand B of restriction fragment Hind L was the only one that started with a guanosine residue. The other strand from Hind L and both from Hind M started with a 5′-terminal adenosine residue. The region Hind L-Hind M cannot be translated in a polypeptide. (16 refs.)

77-3918 **Transcription and Reisolation of the Simian Virus 40 Nucleoprotein Complex.** (Eng.) Hall, M. R. (Dept. Cell and Molecular Biology, Medical Coll. Georgia, Augusta, GA 30902) *Biochem Biophys Res Commun* 76(3): 698-704; 1977.

Simian virus 40 (SV40) DNA and nucleoprotein complexes containing SV40 DNA from SV40-infected CV-1 cells were transcribed in vitro by DNA-dependent RNA polymerase from Escherichia coli. The transcription rate of the DNA in purified nucleoprotein complexes was about 80% less than that of purified viral DNA. Hybridization studies demonstrated that the polymerase made accurate copies of the DNA within the nucleoprotein complexes. The nucleoprotein complexes could be isolated intact after transcription: this is strong evidence that transcription actually occurs on the DNA-protein template rather than on some deproteinized form of DNA. It is concluded that the nucleoprotein complexes, which contain histone proteins and seem to be made up of about 20 nucleosomes, may serve as a model for the study of chromatin transcription. (18 refs.)

77-3919 **Characterization of Components Released by Alkali Disruption of Simian Virus 40.** (Eng.) Christiansen, G. (Dept. Biochemistry, Stanford Univ. Sch. Medicine, Stanford, CA 94305) Landers, T.; Griffin, J.; Berg, P. *J Virol* 21(3): 1079-1084; 1977.

When simian virus 40 (SV40) particles were treated at pH 9.8 with 1 mM dithiothreitol for 5 min at 37 C, the virions were disrupted into a 60S DNA-protein complex and DNA-free 7S protein particles. The DNA-protein complex contained approx equal amounts of DNA and protein and appeared by electron microscopy to be relaxed circular structures with an av of 21 beads joined by short, thin bridges. The major protein components in the complex were host-cell histones, but SV40-specific proteins VP3 and VP2 were also present. The 7S protein particles were almost exclusively VP1 and, in negatively stained samples, they resembled the capsomer structures of intact virions. (14 refs.)

77-3920 **Cell Killing by Simian Virus 40: Impairment of Membrane Formation and Function.** (Eng.) Norkin, L. C. (Dept. Microbiology, Univ. Massachusetts, Amherst, MA 01002) *J Virol* 21(3): 872-879; 1977.

Simian virus 40 (SV40) infection of CV-1 green monkey kidney cells resulted in the release of mitochondrial malic dehydrogenase as early as 24 hr. Released malic dehydrogenase was detected in the cytoplasm prior to its appearance in the overlay medium. Infected cells lost their ability to consume oxygen between 48 and 56 hr, and damage to the electron transport system was indicated. Nevertheless, cellular ATP levels remained high as late as 72 hr after infection. Infection led to a stimulation of membrane phospholipid synthesis which peaked at about 32 hr. This was followed by a severe decline in new membrane synthesis, which correlated in time with the release of cytoplasmic lactic dehydrogenase into the overlay media. Lactic dehydrogenase release preceded the accumulation of trypan blue-stainable cells by about 6 hr Infection had no effect on the turnover of prelabeled membrane phospholipids. An early SV40 mutant, tsA58, and a late mutant, tsB11, were both less effective than wild-type virus in causing reduced levels of phospholipid synthesis, enzyme release, and the accumulation of trypan blue-stainable cells. Another late mutant, tsB8, was similar to wild-type virus in these respects. At 64 hr, there was no detectable cell-associated lactic dehydrogenase and nearly all the cell were trypan blue-stainable. However, at concentrations o deoxyglucose in the medium below the transport Km, deoxyglucose uptake was similar in infected and control cultures

With higher deoxyglucose concentrations in the medium, uptake by the infected cultures exceeded that by the control cultures. (27 refs.)

77-3921 **Characterization of Simian Virus 40 Transformed African Green Monkey Cells (CV-1). I. Defective Virion and Viral Genome.** (Eng.) Hirai, K. (Dept. Molecular Biology, Tokai Univ. Sch. Medicine, Isehara, Japan) *Microbiol Immunol* 21(5): 267-278; 1977.

Several clones of simian virus 40 (SV40)-transformed CV-1 cells were characterized with respect to production of T and V antigens and state of the viral genome. The transformed CV-1 cells failed to produce infectious virions, as shown by sonication or cocultivation and fusion with normal CV-1 cells, and they were resistant to superinfection by SV40. Some clones of the transformed cells contain V antigens. The population of V antigen-positive cells varied from 0% to 100%, depending on the passage number, but the proportion of T antigen-positive cells was always 100%. The virions isolated from the transformed cells were morphologically similar to but lighter in density than complete SV40. In one clone, a small amount of SV40 DNA was detectable in a free state, but a large proportion of the DNA hybridizable with SV40 ^{3}H complementary RNA was linearly integrated into the cell DNA. The free SV40 DNA was noninfectious, closed circular DNA of a size smaller than infectious SV40 DNA component I. Since the cell extracts of the transformed cells contained an agent(s) that induced T and V antigens in normal CV-1 cells, it is suggested that the SV40-transformed CV-1 cells contained free as well as integrated defective SV40 genomes responsible for the synthesis of T and V antigens. (22 refs.)

77-3922 **Transformation by Simian Virus 40 Induces Virus-specific, Related Antigens in the Surface Membrane and Nuclear Envelope.** (Eng.) Lin, P. S. (Tufts-New England Medical Center, Therapeutic Radiology Dept., Radiobiology Div., 171 Harrison Ave., Boston, MA 02111) Schmidt-Ullrich, R.; Wallach, D. F. *Proc Natl Acad Sci USA* 74(6):2495-2499; 1977.

Nucleus- and mitochondrion-free membranes from simian virus 40 (SV40)-transformed hamster lymphocytes, GD248 cells, cause guinea pigs to produce immune sera that reveal the presence in GD248 plasma membranes and mitochondria of two types of glycoprotein that are not detected in membranes of normal lymphocytes. Indirect immune fluorescence of living, SV40-transformed T19 hamster reticulum cells, BALB/c 3T3 mouse fibroblasts, and W18VA2 human fibroblasts, using the antisera against GD248 membrane, produced a distinct cell surface fluorescence at 4C. Above 20C, staining at the nuclear perimeter, the SV40 U-antigen reaction, became equally prominent. In SV40-transformed cells fixed in cold acetone, as well as in purified GD248 nuclei, thermostable U-antigen staining was dramatic, but there was no reaction for nuclear T-antigen. Rabbit antisera against T19 cells gave immunofluorescence reactions equivalent to those obtained with the antisera against GD248 cells. Normal guinea pig or rabbit sera and cells that had not been transformed by SV40 gave no reaction. Sera from tumor-bearing hamsters gave only nuclear T-antigen fluorescence. The results indicate the presence of related, SV40-specific antigens in the surface membranes, nuclear envelope, and possibly other intracellular organelles of SV40-transformed cells. (13 refs.)

77-3923 **Active Amino Acid Transport in Plasma Membrane Vesicles from Simian Virus 40-transformed Mouse Fibroblasts. Characteristics of Electrochemical Na+ Gradient-stimulated Uptake.** (Eng.) Lever, J. E. (Imperial Cancer Res. Fund Labs., Lincoln's Inn Fields, London WC2A 3PX, England) *J Biol Chem* 252(6): 1990-1997; 1977.

Selectively permeable membrane vesicles from SVA31E7, a clonal line of simian virus 40-transformed BALB/c 3T3 fibroblasts, catalyzed Na+ gradient-coupled active transport of several neutral amino acids. Na+-stimulated alanine transport accompanied plasma membrane material during centrifugation in discontinuous dextran 110 gradients. When Na+ was equilibrated across the membrane, countertransport stimulation of ^{3}H-L-alanine uptake occurred in the presence of accumulated unlabeled L-alanine, 2-aminoisobutyric acid, or L-methionine. Competitive interactions among neutral amino acids, pH profiles, and apparent Km values for Na+ gradient-stimulated transport into vesicles suggested that the transport activity assayed in vesicles is part of the corresponding cellular uptake. Both initial rate and quasi-steady state of uptake were stimulated as a function of a Na+ gradient (external> internal) applied artificially across the membrane, independently of endogenous (Na+ + K+)-ATPase activity. Stimulation was decreased when the Na+ gradient was dissipated by monensin, gramicidin D, or Na+ preincubation. Na+ decreased the Km for alanine, 2-aminoisobutyric acid, and glutamine transport. Evidence for an electrogenic mechanism of Na+-dependent amino acid uptake was obtained--uptake was stimulated by conditions expected to create an interior-negative membrane potential, such as the presence of anions with increased permeability to biological membranes and by creation of K+ diffusion potential (internal> external) in the presence of valinomycin. Thus, the net force driving concentrative amino acid uptake is the electrochemical potential of Na+ across the membrane, which is the sum of electrical and chemical thermodynamic parameters. Several possibilities for the regulation of amino acid transport can be predicted by this mechanism. (46 refs.)

77-3924 **Contact-inhibited Revertant Cell Lines Isolated from Simian Virus 40-transformed Cells. VII. Serum Detachment-resistant Revertant Cells.** (Eng.) Bradley, W. E. (Dept. Microbiology, Sch. Medicine, Case Western Reserve Univ., Cleveland, OH 44106) Culp, L. A. *J Virol* 21(3): 1228-1231; 1977.

Flat revertant cells of simian virus 40-transformed BALB/c mouse fibroblasts were isolated on the basis of resistance to a selective detachment procedure using serum and phosphate-buffered saline. In terms of T antigens, chromosome number, saturation density, and density-dependent inhibition of 2-deoxyglucose uptake, the revertants were generally similar to those isolated by other procedures. Their sialic acid content was higher, but this may have been due to the selection procedure. (13 refs.)

77-3925 **Antigenic Distinctions of Glycoproteins in Plasma and Mitochondrial Membranes of Lymphoid Cells Neoplastically Transformed by Simian Virus 40.** (Eng.) Schmidt-Ullrich, R. (Tufts-New England Medical Center, Dept. Therapeutic Radiology, Radiobiology Div., 171 Harrison Ave., Boston, MA 02111) Thompson, W. S.; Wallach, D. F. *Proc Natl Acad Sci USA* 74(2): 643-647; 1977.

Highly purified plasma membranes from hamster lymphocytes (GD 248) transformed by simian virus 40 were compared with the membranes of normal cells by crossed immune electrophoresis, crossed-line immune electrophoresis, and bidimensional isoelectric focusing-immune electrophoresis. Antiserum raised by inoculation of guinea pigs with GD 248 membranes was used as serologic reagent, either directly or after absorption with membranes from normal cells. Bidimensional immune electrophoresis revealed the presence of at least three antigens in the plasma membranes of GD 248 cells that were not detectable in the membranes from normal cells. At least two of these were also present in the mitochondrial membranes of GD 248 cells, but none could be detected in the membranes of embryonic fibroblasts. Bidimensional isoelectric focusing-immune electrophoresis indicated that the distinctive antigens of the GD 248 membranes are glycoproteins. (23 refs.)

77-3926 **Simian Virus 40-Chinese Hamster Kidney Interaction. III. Characteristics of Chemical Induction in a Clone of Virogenic Transformed Cells.** (Eng.) Morris, A. G. (Dept. Biological Sciences, Univ. Warwick, Coventry, Warwickshire CV4 7AL, England) Lavialle, C.; Suarez, H. G.; Stevenet, J.; Estrade, S.; Cassingena, R. *J Gen Virol* 36(1): 123-135; 1977.

The following agents were tested for their ability to induce simian virus 40 (SV40) production in a virogenic clone of SV40-transformed Chinese hamster kidney cells (CHK/SVLP Cl 5.1): mitomycin C (MC), N-methyl-N′-nitro-N-nitrosoguanidine, cycloheximide, 5-iodo-2′-deoxyuridine, dibutryl cAMP, temperature shock, and UV irradiation. MC provided the most effective stimulus of SV40 production and was optimally effective at a concentration of 0.6 μg/ml. Levels of infectious SV40 DNA were increased as early as 6 hr after treatment with MC; max levels were reached after 48 hr. MC stimulated both the virus burst per cell and the proportion of virus-producing cells in the culture. Caffeine, at doses not toxic to noninduced cells, strongly inhibited SV40 production in both noninduced and induced cells, suggesting that DNA repair mechanisms are involved. (32 refs.)

77-3927 **Simian Virus 40 Tumor-specific Proteins: Subcellular Distribution and Metabolic Stability in HeLA Cells Infected with Nondefective Adenovirus Type 2-Simian Virus 40 Hybrid Viruses.** (Eng.) Deppert, W. (Tumor Virology Lab., Salk Inst., San Diego, CA 92112) Walter, G.; Linke, H. *J Virol* 21(3): 1170-1186; 1977.

Several simian virus 40 (SV40)-specific proteins were produced by HeLa cells infected with adenovirus type 2 (Ad2)-SV40 hybrid viruses, including the previously reported 28,000-dalton protein of Ad2+ND1, the 42,000- and 56,000-dalton protein of AD2+ND2, the 56,000-dalton protein of AD2+ND4, and the 42,000-dalton protein of AD2+ND5. In addition, the SV40-specific proteins induced by AD2+ND4 included proteins of 28,000, 42,000, 60,000, 64,000, 72,000, and 74,000 daltons and a doublet of 95,000 daltons. Cell fractionation studies demonstrated that the SV40-specific proteins were detectable in the nuclear, cytoplasmic, and plasma membrane fractions. By pulse-chase and cell fractionation experiments, three classes of SV40-specific proteins were distinguished with regard to metabolic stability: (1) unstable in the cytoplasmic but stable in the nuclear and plasma membrane fractions; (2) stable in the nuclear, cytoplasmic, and plasma membrane fractions; and (3) unstable in all subcellular fractions. Immunoprecipitation of infected cell extracts demonstrated that most of the proteins shared antigenic determinants with proteins expressed in hamsters bearing SV40-induced tumors. Only the 42,000-dalton protein of Ad2+ND5 was not immunoprecipitable. (32 refs.)

77-3928 **Inhibition of DNA Synthesis of Synchronized RSa Cells by Human Leukocyte Interferon.** (Eng.) Fuse, A. (Dept. Microbiology, Sch. Medicine, Chiba Univ., 1-8-1 Inohana, Chiba 280, Japan) Kuwata, T. *J Natl Cancer Inst* 58(4): 891-896; 1977.

A human WBC interferon (IF) preparation suppressed DNA synthesis and subsequent cell division in synchronized RSa cells obtained from human embryonic fibroblasts doubly ransformed by Rous sarcoma virus and simian virus 40.)NA synthesis was inhibited completely when IF (500 U/ nl) was added to cell cultures in the late G_1 phase; the inhibiion was less marked when IF was added in the G_1/S boundiry phase. Overall protein synthesis was reduced only slightly y IF treatment. The results suggest that the critical events eading to the inhibition of DNA synthesis and subsequent ell division by IF take place in late G_1 or S. (25 refs.)

77-3929 **The Arrangement of Nucleosomes in Nucleoprotein Complexes from Polyoma Virus and SV40.** (Eng.) Ponder, B. A. (Dept. Molecular Virology, Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England) Crawford, L. V. *Cell* 11(1): 35-49; 1977.

The arrangement of nucleosomes was examined in relation to the DNA base sequence in nucleoprotein complexes from polyoma virus and simian virus 40 (SV40). The 140-base pair protected DNA fragments from a micrococcal nuclease digestion of a nucleoprotein complex were isolated and redigested with restriction enzymes. Digestion of the 140-base pair DNA with the restriction endonucleases Bam 1 and Eco RI yielded a reproducible series of about 10 smaller fragments. The results suggest that the polyoma and SV40 nucleoprotein complexes contain a repeated element of structure that is continuous throughout the nucleosome and bridge regions. The structure determines both a nonrandom arrangement of the nucleosomes at regularly spaced alternative positions and the spacing of susceptible sites for nuclease digestion in the bridge DNA. (48 refs.)

77-3930 **Nucleotide Sequence Around the Replication Origin of Polyoma Virus DNA.** (Eng.) Soeda, E. (Natl. Inst. Genetics, Mishima 411, Japan) Miura, K.; Nakaso, A.; Kimura, G. *FEBS Lett* 69(2): 383-389; 1977.

The nucleotide sequence of the *Hpa*II-5 fragment of polyoma virus was determined. The fragment is composed of 73 base pairs. A symmetrical adenine-thymidine stretch was flanked by a guanosine-cytosine-rich region with a twofold rotational axis of symmetry. This feature was also observed in simian virus 40 DNA near the origin of replication. (17 refs.)

77-3931 **Immunological Reactivity of Antisera to Sodium Dodecyl Sulfate-derived Polypeptides of Polyoma Virions.** (Eng.) McMillen, J. (Div. Biology, Kansas State Univ., Manhattan, KS 66505) Consigli, R. A. *J Virol* 21(3): 1113-1120; 1977.

Antisera to sodium dodecyl sulfate-derived polyoma virion polypeptides were produced in New Zealand white rabbits. With this antisera, it was possible to detect, by immunofluorescence, the cytoplasmic synthesis of V1, V2, and V3 polypeptides at 18 yr postinfection and their subsequent transport to the nucleus by 22 hr postinfection of mouse kidney cells. Anti-V1, anti-V2, and anti-V3 sera did not react with intact virions in an immunodiffusion assay, nor did they possess hemagglutination inhibition or viral neutralization activity. Antiserum produced against the four host histone polypeptides (V4 through V7) demonstrated immunofluorescence when reacted with polyoma-infected cells but not with uninfected cells. Anti-histone serum was also capable of neutralizing viral infectivity, inhibiting hemagglutination, and reacting with whole virions in an immunodiffusion assay. These results indicate the usefulness of individual polypeptide antibodies for study of the synthesis and assembly of polyoma virions. The data also suggest that histones may be involved in viral functions other than those pertaining to viral DNA conformation. (25 refs.)

77-3932 **Descriptive and Comparative Studies of Type C Virus DNA Polymerase of Fish (Northern Pike, *Esox Lucius*) (Meeting Abstract).** (Eng.) Sonstegard, R. A. (Univ. Guelph, Guelph, Ontario, Canada) Papas, T. S. *Proc Am Assoc Cancer Res* 18: 202; 1977. (no refs.)

77-3933 **Ultrastructure of Two Rat Hepatoma Cell Lines Carrying a C-Type Virus.** (Eng.) Felluga, B. (International Inst. Genetics and Biophysics, Consiglio Nazionale delle Ricerche, Via Marconi 10, 80125 Naples, Italy) Mazza, A.; Gargiulo, M. *J Submicr Cytol* 9(2-3): 145-156; 1977.

The subcellular structure of rat Reuber H-35 hepatoma cells, a clone of cells (Fu5) derived from this hepatoma, and a clonal derivative of Fu5 (Fu5-967), which lacks hypoxanthine-guanine phosphoribosyl transferase, was compared. Particular attention was given to the C-type virus particles abundant in the Fu5 and Fu5-967 cultures. Fu5-967 and Fu5 cells were identical in morphology; both lines had the cultural and ultrastructural properties of hepatic epithelial cells. They differed from the original tumor cells with respect to (1) polar organization; (2) abundance of cytoskeletal elements; (3) prominent exocytic activity of the dense material; and (4) presence of paired cisternae of the endoplasmic reticulum and annular lamellae. The C-type virus particles were present in the Fu5 and Fu5-967 cells in abundance, but they were rarely seen in the original hepatoma cells. The particles appeared identical in shape, size, and morphopoiesis to those seen in H-4 cells. (23 refs.)

77-3934 **Malignant Transformation of Mouse and Rat Cells by BK Virus.** (Eng.) Soriano, F. (Health Central Inst. Education and Cancer Res., Minneapolis, MN 55422) Shelburne, C. E.; Gokcen, M. *IRCS Med Sci: Cancer* 5(7): 338; 1977.

In an investigation of the carcinogenicity of BK virus, the virus was recovered from CS cells, a line obtained from tumors that developed in hamsters after BK virus inoculation. Swiss-Webster mouse and Sprague-Dawley rat primary embryo cultures were then transformed by the rescued virus. This may indicate selection of more oncogenic viral genomes in the tumor. (3 refs.)

77-3935 **Evidence for Recombination Between N- and B-Tropic Murine Leukemia Viruses.** (Eng.) Hopkins, N. (Center Cancer Res., Massachusetts Inst. Technology, Cambridge, MA 02139) Schindler, J.; Gottlieb, P. D. *J Virol* 21(3): 1074-1078; 1977.

When Sc-1 cells were coinfected with N- and B-tropic murine leukemia viruses, that differ in their XC plaque morphology, viruses designated XLP-N, were obtained that appeared to be recombinants, since they possessed the N tropism of one parent and the XC plaque morphology of the other (B-tropic virus) parent. Evidence, based on antigenicity and electrophoretic mobility, that some clonal isolates of XLP-N have inherited the gp70 gene of their B-tropic virus parent is presented. In addition to demonstrating that XLP-N viruses are recombinants, the fact that an N-tropic virus may possess a gp70 derived from a B-tropic virus proves that the N or B tropism of murine leukemia viruses does not reside in gp70. (20 refs.)

77-3936 **Titration of Murine Leukemia Viruses with Rat Cell Line RFL.** (Eng.) Koga, M. (Dept. Pathology, Cancer Res. Inst., Faculty Medicine, Kyushu Univ., Fukuoka, Japan) *J Virol* 23(2): 436-438; 1977.

A direct assay, in which the number of syncytium foci formed in the infected cells are counted, was found to be a sensitive measure of the infectivity of murine leukemia virus. Apparently the syncytia are formed as a cytopathic effect after infection. (11 refs.)

77-3937 **DNA Transfection of Ecotropic Murine Leukemia Viruses in Mouse Cell Cultures.** (Eng.) Hsu, I. C. (Experimental Pathology Branch, NCI, NIH, Bethesda, MD 20014) Yang, W. K. *Cancer Res* 37(6): 1709-1714; 1977.

DNA's isolated from cells chronically infected with ecotropic (N-, B-, and NB-tropic) murine leukemia viruses (MuLV) were tested for infectivity in mouse NIH3T3, BALB/c3t3 clone A31, SV-A31, BALB-ME, and N-SME cultured cells using an XC plaque assay. The apparent dose causing 50% infection under most experimental conditions was 0.3 μg. Hydrocortisone treatment (10^{-6} M) facilitated early detection of transfection in DNA-infected cells. Shearing of DNA solutions (30-50 μg/ml) by forcing them through a 25-gauge needle 6-10 times before and after calcium chloride precipitation made quantitative inoculation possible and increased the efficiency of transfection to a max. With the combined use of optimal DNA size and hydrocortisone in the medium, transfection could be obtained in a relatively short time; ie, within days instead of weeks. Susceptibility to MuLV DNA transfection was not related to sensitivity to MuLV virion infection in the mouse cell cultures. In NIH3T3 and SV-A31 cells carrying restriction alleles of *Fv-1* locus against the viruses, horizontal transmission was inhibited on subsequent passages. Progeny MuLV from transfected cells had N- or B-tropic properties similar to those of the parent MuLV. (25 refs.)

77-3938 **Mechanism of Restriction of Ecotropic and Xenotropic Murine Leukemia Viruses and Formation of Pseudotypes Between the Two Viruses.** (Eng.) Besmer, P. (Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA 02139) Baltimore, D. *J Virol* 21(3): 965-973; 1977.

Ecotropic and xenotropic murine leukemia viruses (MuLV's) constitute separate interference groups; within each group there is cross-interference, but between the groups there is no detectable interference. Interference is manifest against pseudotypes containing the vesicular stomatitis virus genome within the coat of one of the MuLV's. The pseudotypes show the cell specificity of the leukemia viruses. Pseudotypes with an ecotropic MuLV coat infect mouse cells but not rabbit or mink cells; pseudotypes with a xenotropic MuLV coat infect rabbit or mink cells well but mouse cells very poorly. Efficient pseudotype formation also occurs between the two MuLV classes, and both the interference patterns and the cell specificity of these pseudotypes are determined entirely by their envelope. Using these pseudotypes, ecotropic MuLV infection could be established in xenogeneic cells, and the resulting progeny could be scored by a conventional XC cell assay. Also, xenotropic intracellular MuLV infection could be established in a mouse cell, showing that no absolute intracellular barrier against xenotropic virus growth exists in murine cells. The major barriers against both xenotropic and ecotropic MuLV therefore are cell surface barriers. Xenogeneic cells probably lack receptors for ecotropic MuLV, but murine cells may either lack receptors for xenotropic MuLV or have receptors that are blocked by endogenous expression of the glycoprotein of endogenous xenotropic MuLV. (47 refs.)

77-3939 **Isolation of Transforming Murine Leukemia Viruses from Mice with a High Incidence of Spontaneous Lymphoma.** (Eng.) Staal, S. P. (Lab. Viral Diseases, Natl. Inst. Allergy and Infectious Diseases, NIH, Bethesda, MD 20014) Hartley, J. W.; Rowe, W. P. *Proc Natl Acad Sci USA* 74(7): 3065-3067; 1977.

Two strains of murine leukemia virus (MuLV) capable of malignant transformation of mink lung tissue culture cells (ATCC no. CCL-64) were isolated. The initial isolate of strain T-8 virus was from an in vitro thymoma cell line, AKT-8, from a spontaneously lymphomatous AKR/J mouse. Strain M-44 virus was isolated from a spontaneous reticulum cell sarcoma in an NIH mouse partially congenic for the *Akv-2* ecotropic MuLV-inducing gene of AKR. Malignant transformation was demonstrated in infectious center assays with mitomycin C-treated cells: focus induction in fluorescent antibody assays. In addition, mink cells inoculated with either strain of virus formed multiple large colonies in agar, but none were produced by uninoculated control cells or cells infected with prototype mink cell focus-inducing virus. The T-8 strain is replication-defective, allowing selection of a transformed nonproducer clonal cell line from which transforming pseudotypes can be obtained. These transforming viruses may play a role in the development of spontaneous virus-induced murine tumors. (13 refs.)

77-3940 **A New Class of Murine Leukemia Virus Associated with Development of Spontaneous Lymphomas.** (Eng.) Hartley, J. W. (Lab. Viral Diseases, Natl. Inst. Allergy and Infectious Diseases, NIH, Bethesda, MD 20014) Wolford, N. K.; Old, L. J.; Rowe, W. P. *Proc Natl Acad Sci USA* 74(2): 789-792; 1977.

A new type of murine leukemia virus has been detected in the thymuses of leukemic and late preleukemic AKR mice, in lymphomas developing in NIH Swiss mice carrying the AKR ecotropic virus-inducing loci *Akv*-1 or *Akv*-2, and in the thymus of a preleukemic C58 mouse. The viruses induce focal areas of morphologic alteration in a mink lung cell line and are tentatively referred to as "mink cell focus-inducing" (MCF) strains. They have the host range of both xenotropic and N-tropic ecotropic murine leukemia viruses, are neutralized by antisera to both ecotropic and xenotropic viruses, and are interfered with by both viruses. They may represent a particular type of genetic recombinant that emerges during the preleukemic period in high-ecotropic-virus mouse strains, and they may play a significant role in the etiology of spontaneous lymphomas. (24 refs.)

77-3941 **Expression of AKR Murine Leukemia Virus gp71-like and BALB(X) gp71-like Antigens in Normal Mouse Tissues in the Absence of Overt Virus Expression.** (Eng.) McClintock, P. R. (Basic Res. Program, NCI, Frederick Cancer Res. Center, Frederick, MD 21701) Ihle, J. N.; Joseph, D. R. *J Exp Med* 146(2): 422-434; 1977.

Two antigens, one serologically indistinguishable from AKR murine leukemia virus gp71 and another indistinguishable from BALB(X) gp71, were found in normal mouse sera of several strains. This suggests that the expression of these antigens is necessary for differentiation or normal cell function. (22 refs.)

77-3942 **Separation of the Moloney Leukemia Virus-determined Cell Surface Antigen (MCSA) from Known Virion Proteins Associated with the Cell Membrane.** (Eng.) Siegert, W. (Dept. Tumor Biology, Karolinksa Institutet, S 10401 Stockholm 60, Sweden) Fenyo, E. M.; Klein, G. *Int J Cancer* 20(1): 75-82; 1977.

Cell membranes of YAC lymphoma cells originally induced in a mouse by Moloney leukemia virus (MLV) were solubilized with NP40. The antigenicity of the solubilized protein fraction was assayed by inhibition of the corresponding cytotoxic reaction against YAC target cells. The MLV-determined cell surface antigen (MCSA) was detected with antisera produced by the repeated injection of heavily irradiated YAC cells into syngeneic mice. Virion proteins gp71, p30, p15, p12, and p10 were identified with goat or rabbit antisera against purified Rauscher and Friend leukemia virus proteins. MCSA bound to concanavalin A-Sepharose was eluted by mannoside together with H-2a and gp71. In contrast, p30, p12, p10, and part of p15 and p15(E) were not retained on the column and could be separated from MCSA. Passage of the glycoprotein fraction through Sephadex G-200 led to the separation of MCSA activity from gp71 and H-2a. MCSA eluted between the IgG and the bovine serum albumin size markers. MCSA could be also separated from the known viral proteins and from H-2 by velocity centrifugation in sucrose gradients. It sedimented (6.6S) ahead of gp71 (4.4S) and H-2 (3.2S). MCSA has approx molecular wt of 110,000 and appears distinct from the known viral proteins gp71, p30, p15(E), p12, and p10 and from H-2. (29 refs.)

77-3943 **Low-Molecular-Weight RNAs of Moloney Murine Leukemia Identification of the Primer for**

RNA-directed DNA Synthesis. (Eng.) Peters, G. (Dept. Physiological Chemistry, Univ. Wisconsin, Madison, WI 53706) Harada, F.; Dahlberg, J. E.; Panet, A.; Haseltine, W. A.; Baltimore, D. *J Virol* 21(3): 1031-1041; 1977.

To determine whether other viruses use transfer RNA's (tRNA's) as primers, the small RNA's of Moloney murine leukemia virus (M-MuLV) were analyzed. These RNA's were fractionated into at least 15 species by two-dimensional polyacrylamide gel electrophoresis. The pattern of the small RNA's was significantly different from that of Rous sarcoma virus. A subset of the virion small RNA's was associated with the genome RNA in the 70S complex. One of the associated molecules, a cellular tRNA, was tightly bound to the genome RNA and served as the major primer for M-MuLV RNA-directed DNA synthesis in vitro. (28 refs.)

77-3944 **Specificity and Distribution of the Determinants of the Major Glycoprotein (gp71) of Murine Oncornaviruses as Detected by an In Vitro Cytotoxicity Assay.** (Eng.) Collins, J. J. (Dept. Surgery, Duke Univ. Medical Center, Durham, NC 27710) Bollio, L. D.; Denny, T. P.; Bolognesi, D. P. *J Natl Cancer Inst* 59(1): 99-106; 1977.

The involvement of the various determinants (type, group, and interspecies) of the major envelope glycoprotein gp71 of murine C-type viruses in rendering cells susceptible to lysis by heterologous anti-gp71 antisera was investigated. The ^{14}C-nicotinamide-release microcytotoxicity assay demonstrated that the lytic activity of rabbit anti-Friend murine leukemia virus (anti-F-MuLV) gp71 serum for mouse cells releasing very high levels of F-MuLV could be neutralized by absorption of the group, but not the interspecies, reactivity of this serum. Rabbit anti-F-MuLV gp71 serum with considerable residual-specific reactivity after appropriate cell absorptions was not lytic for the F-MuLV-releasing cells. In addition to successful absorptions with mouse cells releasing F-MuLV, Gross murine leukemia virus, or AKR murine leukemia virus, normal mouse embryo cells also could remove the cytotoxic reactivity of the rabbit anti-F-MuLV gp71 serum. The presence of a molecule in normal cells bearing a gp71 grouplike determinant was confirmed by the ability of cell extracts to block the specific precipitation of purified gp71 in competition radioimmunoassay. The results suggest that the group determinant of gp71 was of major importance in the cytotoxic reaction and that such a determinant was also present on normal mouse cells, probably reflecting the expression of endogenous virus. (6 refs.)

77-3945 **Friend Virus-Induced Inhibition of Eosinophil Response to Antigen: Requirement for Complete Virus (Meeting Abstract).** (Eng.) McGarry, M. P. (Roswell Park Memorial Inst., Buffalo, NY 14263) Styles, B. D.; Mirand, E. A. *Proc Am Assoc Cancer Res* 18: 178; 1977. (no refs.)

77-3946 **Spleen Colony Formation in Mice by Friend Leukemia Cells: A Result of Donor or Host Cell Proliferation (Meeting Abstract)?** (Eng.) Steeves, R. (Albert Einstein Coll. Medicine, Bronx, NY 10461) Steinheider, G.; Lilly, F. *Proc Am Assoc Cancer Res* 18: 71; 1977. (no refs.)

77-3947 **Characterization of Molecular Species Carrying Gross Cell Surface Antigen.** (Eng.) Snyder, H. W. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021) Stockert, E.; Fleissner, E. *J Virol* 23(2): 302-314; 1977.

The Gross cell-surface antigen (GCSA), associated with expression of endogenous Gross-type murine leukemia virus (G-MuLV) in tissues of mice, is defined by the cytotoxic reaction of a C57BL/6 antiserum, anti-AKR spontaneous leukemia K36, with cells of the Gross virus-induced C57BL/6 leukemia E male G2. Sequential lactoperoxidase-catalyzed radioiodination of E male G2 cells, Nonidet P-40 lysis, precipitation with anti-K36 serum, and sodium dodecyl sulfate-polyacrylamide gel electrophoresis identified molecules with properties of polyproteins encoded by the *gag* region of the viral genome. These cell-surface species could also be labeled by in vitro culturing of E male G2 with radioactive glucosamine. The The viral specificity of these molecules and their participation in the GCSA typing system were established as follows: (1) Absorption of anti-K36 serum with GCSA+, but not GCSA-, leukemias led to a marked decrease in precipitation of these proteins. (2) The same E male G2 cell surface proteins were also precipitated by antisera against the MuLV virion proteins p30 and p15. (3) Anti-K36 was shown to possess antibodies against Gross virus p30 and p15. (4) "Clearing" the E male G2 lysate of molecules reactive with anti-p30 or anti-p15 sera removed molecules reactive with anti-K36. Absorption of anti-K36 serum with disrupted G-MuLV virions or with Gross p30 or p15 removed GCSA cytotoxic antibodies; partial absorption was achieved with disrupted Rauscher-MuLV (R-MuLV) or with R-MuLV p30, but no absorption was found with R-MuLV p15. These data show that E male G2 cells express, on their surfaces, MuLV core polyproteins that apparently can be glycosylated and on which the determinants of GCSA are located. (59 refs.)

77-3948 **Propagation of a B-tropic Murine Leukemia Virus in N-Type Cells in the Presence of Differ-**

ent Murine Sarcoma Viruses. (Eng.) Yoshikura, H. (Dept. Genetics, Inst. Medical Science, Univ. Tokyo, Post Office Takanawa, Tokyo, Japan) Catala, F. *Intervirology* 8(5): 319-322; 1977.

The host range of the progeny obtained after propagating a B-tropic murine leukemia virus (MuLV) in N-type cells in the presence of three strains of murine sarcoma virus (MuSV: S+l-, Harvey, or Kirsten MuSV) was examined. The normal mouse cell lines used were N-type MLg and C3H2K cells, B-type YH-7 cells, and SC-1 cells permissive to both N- and B-tropic viruses. For the rescue of MuSV, S+L- C182, Harvey MuSV-transformed BALB/c mouse cells were infected with a B-tropic MuLV, WN1802B, at a multiplicity of about 1, and the virus progeny in the supernate were propagated further in the YH-7 cells. WN1802B was converted to NB-tropic virus after 5 days of propagation in the nonpermissive MLg or C3H2K cells in the presence of S+L- MuSV, but not in the presence of Harvey or Kirsten MuSV. B-tropic virus may still exist in the progeny of S+L-MuSV(WN1802B) propagated in MLg or C3H2K cells, as the ratio of the plaquing efficiencies in N-type cells to B-type cells was still < 1. However, in assays of 12 clones of the virus propagated in MLg cells, all were considered NB-tropic. (9 refs.)

77-3949 **Differences and Similarity in RNA Regulation in Tumors Induced by Chemical Compounds and by RNA- and DNA-Containing Viruses.** (Rus.) Shearer, R. V. (USA) *Vestn Akad Med Nauk SSSR* (3): 69-74; 1977.

The differences between virus-induced tumors and tumors induced by chemical carcinogens were studied by competitive hybridization. Gene derepression was observed in Kirsten virus-induced rat lymphomas, but not in azo dye-induced hepatomas. Both virally and chemically induced tumors lost their selective nucleus-to-cytoplasm transport of RNA. (13 refs.)

77-3950 **A Comparison of Membrane Components of Normal and Transformed BALB/c Cells.** (Eng.) Van Nest, G. A. (Dept. Biochemistry, Coll. Medicine, Univ. Arizona, Tucson, AZ 85724) Grimes, W. J. *Biochemistry* 16(13): 2902-2908; 1977.

Membrane glycolipids, glycoproteins, and surface proteins of normal and transformed BALB/c cell lines were compared. Several virally (Moloney murine sarcoma virus) and spontaneously transformed cell lines showed differences in membrane component compared with A_{31} cells. These differences consisted of increased amounts of the more simple gangliosides, absence of the large external transformation-sensitive (LETS) protein, and the appearance of a major new glycoprotein band of about 105,000 molecular wt. In contrast, the spontaneously transformed cell line (3T12T) that caused the fastest growing tumors in vivo and the most rapid animal death did not have these changes. The A_{31} and 3T12T glycolipid profiles were similar, as were glycoproteins and cell surface proteins detected by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. When pronase-generated glycopeptides were analyzed by Sephadex G-50 chromatography, an enrichment in the faster-eluting species was seen in two killing tumor lines (c5T and 3T12T) compared with A_{31}. Regressing tumor lines (Moloney transformed, c5) did not show this change. Isolated membrane glycoproteins yielded glycopeptides of different sizes after pronase digestion. In addition, several 3T12T glycoproteins yielded glycopeptides larger than those from the corresponding glycoproteins of A_{31} cells. It appears that glycopeptide alterations associated with transformation occur in several membrane glycoproteins. (29 refs.)

77-3951 **Lack of Growth of a Pregnancy-dependent Mouse Mammary Tumor (TPDMT-4) in the Absence of Pituitary Hormones.** (Eng.) Matsuzawa, A. (Lab. Animal Res. Center, Inst. Medical Science, Univ. Tokyo, Takanawa Post Office, Tokyo 108, Japan) Yamamoto, T. *J Natl Cancer Inst* 58(4): 1087-1091; 1977.

Mammary tumors of a transplantable, pregnancy-dependent line (TPDMT-4) established in DDD mice are characterized by growth during pregnancy and regression after parturition. This results in higher growth peaks in subsequent pregnancies in breeders and no growth in virgins. The effect of hypophysectomy on tumor growth in mice given 17β-estradiol (E, 0.16 mg), progesterone (P, 39.92 mg), or deoxycorticosterone acetate (DCA, 39.92 mg) was investigated. Growth of cancers occurred in E+P- and E+DCA-treated virgins, but not in cholesterol-treated (50 mg) virgins.. Tumors did not grow to palpable sizes in cholesterol-, E+P-, and E+DCA-treated hypophysectomized virgins; this indicated that pituitary hormones were essential for tumor growth. Impalpable but microscopic tumors were obtained at necropsy in 1/5 cholesterol-treated, 5/10 E+P-treated, and 3/6 E+DCA-treated hypophysectomized animals. The neoplasms showed ductal and tubular structures that were lined by a single layer of well-differentiated cuboidal epithelium, which suggested that the tumor line might be derived from ductal cells. (15 refs.)

77-3952 **Leukocyte Migration Inhibition in Human Breast Cancer with Mouse Mammary Tumor Virus, GP-52 and GP-70 (Meeting Abstract).** (Eng.) McCoy, J. (NCI, Bethesda, MD 20014) Dean, J. H.; Herberman, R. B. *Proc Am Assoc Cancer Res* 18: 177; 1977. (no refs.)

77-3953 **Paternal Transmission of Mammary Tumor Virus from DD/Tbr Strain of Mice by Crossing BALB/c or C57BL/6J Strains.** (Eng.) Tsubura, Y. (Dept. Pathology, Nara Medical Coll., 840 Shiji-cho, Kashihara, Nara-ken 634, Japan) *Gann* 68(3): 257-266; 1977.

Crosses between mice (DD/Tbr) with a high incidence of mammary tumors and mice (BALB/c or C57BL/6J) with a low incidence showed that mammary tumor virus (MTV) is transmitted paternally. DD/Tbr (D) mice developed mammary tumors (77.7% incidence) at an av age of 9.3 mo in F_{44} to F_{56} generations. Hybrids of D and BALB/c (C) developed mammary tumors with identical incidence in both reciprocal crosses: 66.7% incidence at an age of 16.4 mo in DCF_1 and CDF_1. In hybrids of D and C57BL/6J (B), mammary tumor incidence was 90.8% in DBF_1 and 84.2% in BDF at an av age of 8.7 and 8.9 mo, respectively. Hybrids of D and B mice were more susceptible to DD/Tbr MTV than hybrids of D and C. Mammary tumors from these hybrid mice demonstrated B-type particles, suggesting that DD/Tbr MTV was transmitted either maternally or paternally. Plaque-inducing ability and paternal transmission are specific for DD/Tbr and GR mice, but the mammary tumor age in DD/Tbr mice is higher than that of GR mice who carry MTV-P. RIII mice have a plaque-inducing ability, but fail to transmit their MTV (MTV-PS) by the paternal route. Therefore, DD/Tbr MTV has characteristics intermediate between MTV-P and MTV-PS. (50 refs.)

77-3954 **Interaction Between Murine RNA Tumor Viruses and Vesicular Stomatitis Virus (VSV) (Meeting Abstract).** (Eng.) Chan, J. C. (M. D. Anderson Hosp. and Tumor Inst., Univ. Texas System Cancer Center, Houston, TX 77030) Hixson, D. C.; Bowen, J. M. *Proc Am Assoc Cancer Res* 18: 30; 1977. (no refs.)

77-3955 **Transformation of X/CF Mouse Embryo Cell Cultures Treated With Iododeoxyuridine (Meeting Abstract).** (Eng.) Goldfeder, A. (Cancer and Radiobiology Res. Lab., Dept. Biology, New York Univ., New York, NY 10032) Stadler, U. *Proc Am Assoc Cancer Res* 18: 111; 1977. (no refs.)

77-3956 **In Vitro Transcription of Wound Tumor Virus RNA by Virion-associated RNA Transcriptase.** (Eng.) Reddy, D. V. (International Crops Res. Inst. for Semi-Arid Tropics, 1-11-256, Begumpet, Hyderabad-500 016, A.P., India) Rhodes, D. P.; Lesnaw, J. A.; Macleod, R.; Banerjee, A. K.; Black, L. M. *Virology* 80(2): 356-361; 1977.

Wound tumor virus virion-bound polymerase can synthesize all 12 single-stranded RNA copies of the genome segments in vitro. The electrophoretic profile of these products is identical to that of the native viral genome. The physical properties are described. (19 refs.)

77-3957 **Isolation and Replication of Mutant Populations of Wound Tumor Virions Lacking Certain Genome Segments.** (Eng.) Reddy, D. V. (International Crops Res. Inst. for Semi-Arid Tropics, 1-11-256, Begumpet, Hyderabad-500 016, A.P., India) Black, L. M. *Virology* 80(2): 336-346; 1977.

Techniques by which purified segments of wound tumor virus from plants were isolated are described. Segments 2, 5, and 7 and the fragments of 11 other segments were isolated. (24 refs.)

See also:

* (Rev.): 77-3601, 77-3647, 77-3648, 77-3649, 77-3650
77-3651, 77-3652, 77-3653, 77-3654, 77-3655, 77-3656
77-3657, 77-3658, 77-3659, 77-3660, 77-3661, 77-3662
77-3674.
* (Chem.): 77-3816.
* (Phys.): 77-3848.
* (Immun.): 77-3959, 77-3960, 77-3961, 77-3963, 77-3964
77-3980, 77-3984, 77-3985, 77-3987, 77-3988, 77-3989
77-3990, 77-3991, 77-3992, 77-3993, 77-3994, 77-3995
77-3997, 77-3998, 77-4006, 77-4007, 77-4008, 77-4009
77-4010, 77-4013, 77-4014, 77-4015, 77-4024, 77-4025.
* (Path.): 77-4102, 77-4108, 77-4118, 77-4119.
* (Epid.-Biom.): 77-4126.

77-3958 **Primary Tumor Immunity in Nude Mice.** (Eng.) Prehn, L. M. (Jackson Lab., Bar Harbor, ME 04609) Outzen, H. C. *Int J Cancer* 19(5): 688-691; 1977.

An investigation was made to determine whether nude mice (nu/nu, partially bred onto a BALB/c background) can be rendered resistant to tumor challenge by previous immunization and whether they show any primary response to tumor antigen recognition. For the latter, the growth of tumor grafts of differing immunogenicities was compared in adult nonirradiated, adult sublethally irradiated, or newborn nude mice. The tumors used were induced in BALB/c mice by 3-methylcholanthrene. The nude mice could not be immunized against any of the tumors, whether they were highly (No. 2361), weakly (No. 2371) or not immunogenic (No. 2373) in normal BALB/c mice. Thus, if nude mice have some T-cell-mediated immune function, it is not strong enough to produce a detectable secondary resistance to any of these tumors. However, despite the lack of a secondary response, the adult nonirradiated nude mice resisted the growth of the highly immunogenic primary tumor grafts (No. 2361 and No. 2371 in first passage), although resistance was not as strong as that in the BALB/c mice. No significant resistance was seen to tumors that were of moderate or weak immunogenicity. The mechanism of this primary radiosensitive tumor resistance in nude mice remains to be determined. It could be purely IgM-mediated (since the IgM response in nude mice is almost normal), or it could be the result of a "leaky" T-cell response, despite the lack of a detectable secondary immunity in the mice. (12 refs.)

77-3959 **Reactivity to SV40 T Antigen in Athymic (Nude), Antithymocyte Serum-treated, and Normal Mice.** (Eng.) Knowles, B. B. (Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA 19104) Ford, S. R.; Aden, D. P. *J Immunol* 119(1): 79-119; 1977.

The possibility that helper T cells are necessary for an immune response to simian virus 40 (SV40) T antigen was investigated. Antisera prepared in syngeneic mice (CBA-T6J, BALB/c, and 129/J) by hyperimmunization with intact SV40-transformed mouse cells or with somatic cell hybrids between SV40-transformed human and normal mouse cells exhibited anti-SV40 T antigen reactivity. Sera from athymic mice bearing tumors formed by SV40-transformed mouse, human, or mouse-human hybrid cells were not reactive with SV40 T antigen. Antithymocyte serum (ATS)-treated mice also lacked T antigen reactivity during suppressive treatment, but they developed antibody to T antigen after ATS treatment was discontinued, at the time of obvious tumor rejection. It is concluded that the presence of growing tumors in the mouse is not necessary for the production of anti-SV40 T antigen antibodies, but that helper thymus-derived cells are essential for the humoral response. (30 refs.)

77-3960 **Direct Comparison of Three Isotopic Release Microcytotoxicity Assays as Measures of Cell-mediated Immunity to Gross Virus-induced Lymphomas in Rats.** (Eng.) Oldham, R. K. (Div. Oncology, Dept. Medicine, Vanderbilt Univ. Hosp., Nashville, TN 37232) Ortaldo, J. R.; Holden, H. T.; Herberman, R. B. *J Natl Cancer Inst* 58(4): 1061-1067; 1977.

Three isotopic release microtoxicity assays--^{125}I-iodo-2′-deoxyuridine release assay (IRA), ^{51}Cr-release assay (CRA), and ^{3}H-proline-release assay (PRA)--were used to measure cell-mediated immunity to (C58NT)D, a Gross virus-induced lymphoma in W/Fu rats. All three assays were done under physical conditions as comparable as possible. A considerable difference was noted in the ability of one or another target cell to function well in each assay. The (C58NT)D tissue culture line was an excellent target cell in the long-term assays, but the ascites line was inadequate. The monolayer Gross virus-induced tumor cell line ERTh/V-G was resistant to lysis in the short-term CRA, but it functioned well in the long-term assays. The autologous and thymus cells were reasonably neutral baseline controls for the evaluation of both normal and immune activity. Although all three assays were capable of measuring both natural and immune activity in this system, the PRA appeared more sensitive at 24 hr and the IRA at 48 hr; the CRA activity with these target cells was useful only in the short-term assays. (40 refs.)

77-3961 **Natural Immunity to Murine Mammary Tumor Viruses.** (Eng.) Bentvelzen, P. (Radiobiological Inst. TNO, Rijswijk, Netherlands) Creemers, P. C. *Contemp Top Immunobiol* 6: 229-238; 1977.

The results of recent studies of immunity to murine mammary tumor viruses (MTV) are reviewed. Using indirect immunofluorescence, antibodies to MTV were found in mammary tumor cultures derived from primary GR mouse tumors harboring the virus strain MTV-P and from tumors induced in BALB/c mice by the endogenous strain MTV-O. In addition, sera from tumor-bearing BALB/c mice had antibodies that gave a broad cross-reactive membrane fluorescence with GR mammary tumor cells. Mice with tumors > 4.0 g showed no detectable antibodies. When mouse sera were incubated overnight at 4 C with purified standard MTV (0.01 mg/0.1 ml serum), cytoplasmic fluorescence was completely abrogated but membrane fluorescence was not. Thus, a nonvirion MTV-associated antigen may be present at the cell surface. (54 refs.)

77-3962 **Killer Cells Reactive to Altered-Self Antigens Can Also Be Alloreactive.** (Eng.) Bevan, M. J. (Center Cancer Res., Massachusetts Inst. Technology, Cambridge, MA 02139) *Proc Natl Acad Sci USA* 74(5): 2094-2098; 1977.

The relationship between reactions to altered-self targets and to targets that bear foreign histocompatibility (H-2) antigens (alloreactions) was investigated. F_1(Balb/c x Balb.B) (H-2d/b) cytotoxic T lymphocytes (CTL) reactive to the minor H differences of B10.D2(H-2d) were positively selected for by in vivo and in vitro immunization with B10.D2. These effectors showed a small degree of cross-reactive lysis of Balb.K(H-2k) targets. The cells lysing Balb.K were selected for further by repeated stimulation in long-term mixed lymphocyte cultures with Balb.K. A highly selected CTL population capable of lysing B10.D2 and Balb.K targets almost equally was obtained. The same killer cell could lyse either target, as indicated by the finding that the rate of lysis of labeled B10.D2 targets was specifically inhibited by addition of an excess of unlabeled Balb.K targets (cold-target competition experiments). Similarly, lysis of the labeled Balb.K targets was inhibited in the presence of B10.D2 targets. The results show that one killer cell can respond to foreign cells that are antigenic because of differences either at minor H loci or at major H loci. (29 refs.)

77-3963 **Virus-induced Autoimmunity Phenomena in Experimental Animals.** (Ger.) Sprossig, M. (Institut fur Medizinische Mikrobiologie der Medizinischen Akademie Erfurt, DDR-50 Erfurt, Nordhauser Strasse 74, E. Germany) Wutzler, P.; Farber, I.; Schweizer, H.; Schneider, J. *Exp Pathol (Jena)* 13(1): 52-57; 1977.

After im and ip immunization of rabbits with autologous testes cells infected with herpes virus hominis types 1 and 2, histologically homogeneous eosinophilic PAS-positive substances were detected in 14/15 animals, mainly in the interstitium of the testes. These substances corresponded to the globulin deposits demonstrated by the reaction of labeled antirabbit globulin. Testes sections of five rabbits inoculated with noninfected autologous cells did not react. On the 28th day postinfection, the antibody levels against virus antigen were 1:32 to 1:1,204. Antibodies against autologous testes cells occurred only after removal of the second testis. The negative findings in the controls indicated that the immunogenicity of the autologous testes cells was not influenced by cultivation or passage conditions. Consequently, a causal connection can be inferred between virus infection and the appearance of autoantibodies. (15 refs.)

77-3964 **Allostimulation of Autocytotoxicity to EBV-Transformed Cell Lines (Meeting Abstract).** (Eng.) Seeley, J. (UCLA Div. Surgical Oncology, Los Angeles, CA 90024) Golub, S. H. *Proc Am Assoc Cancer Res* 18: 174; 1977. (no refs.)

77-3965 **Blocking Factors Against Leucocyte-dependent Melanoma Antibody in the Sera of Melanoma Patients.** (Eng.) Murray, E. (Kanematsu Memorial Inst., Sydney Hosp., Sydney, New South Wales 2000, Australia) McCarthy, W. H.; Hersey, P. *Br J Cancer* 36(1): 7-14; 1977.

In previous studies, in which plasmapheresis was used to remove blocking factors of cell-mediated cytotoxicity to melanoma cells from the circulation of melanoma patients, it was suggested that leukocyte-dependent antibody (LDA) to melanoma cells may also be blocked by factors in the sera of these patients. The present study confirms these findings by showing that 7/8 patients with disseminated melanoma had melanoma LDA activity in the IgG fraction of their sera. This also applied to 4/8 patients with primary melanoma. Evidence that the blocking factors may be immune complexes was provided by experiments in which LDA activity to melanoma cells was revealed after acidification of melanoma sera to dissociate immune complexes, followed by ultrafiltration through membranes retaining molecules > 100,000 daltons. Blocking of LDA activity in the retentate recurred when the retentate was recombined with the filtrate. Further studies indicated that the blocking activity was directed to the target cell and not the effector cell. Preliminary analysis of the specificity of the blocking suggests that it was similar to that of melanoma antisera. These results suggest that blocking of LDA activity to melanoma cells is common in melanoma patients and that their quantitative analysis may yield information of biological importance in the management of these patients. (24 refs.)

77-3966 **Inhibition of Leukocyte Chemotaxis by Homogenates of Tumor Tissues.** (Eng.) Hamby, C. V. (Dept. Microbiology, Univ. Missouri, Columbia, MO 65201) Barrett, J. T. *Oncology* 34(1): 13-15; 1977.

The effects of tissue homogenates of various human tumors on the motility of eosinophilic and neutrophilic WBC in guinea pig peritoneal exudates was studied. Homogenates of liver melanoma, vertebral melanoma, mammary duct cancers, and lymphosarcoma inhibited both neutrophil and eosinophil motility. A lung carcinoma homogenate inhibited neutrophil migration, but had no effect on eosinophil migration. A liver cancer homogenate was chemotactic for neutrophils but had no effect on eosinophil migration. It is suggested that antichemotactic factors produced by tumor cells could conceivably thwart an inflammatory immune response against tumor cell growth. (8 refs.)

77-3967 **Facilitation of DMBA-induced Tumor Invasion by Antilymphocyte Serum.** (Eng.) Gardner, H. A. (Dept. Pathology, Univ. Toronto, 2075 Bayview Ave., Toronto, Ontario, Canada M4N 3M5) Kellen, J. A. *J Clin Hematol Oncol* 7(3): 843-848; 1977.

Mammary tumors were induced by three consecutive iv injections of 2 mg dimethylbenz(a)anthracene (DMBA) on the 50th, 53rd, and 56th days of life into Sprague-Dawley female rats. Horse anti-rat lymphocyte serum (ALS) was administered ip in 0.5-ml aliquots at various time intervals to assess its action on tumor growth. The degree of inflammatory reaction was definitely decreased in tumors derived from ALS-treated animals. In rats treated concomitantly with ALS and DMBA, 3/8 neoplasms showed tumor infiltration into the underlying pectoral muscle. Alteration of the tumor growth pattern by immunosuppression with ALS was demonstrated, because the tumor model used is antigenic and rarely metastasizes. Thus, impairment of the cellular immune response enhanced invasive spread of the tumor. (8 refs.)

77-3968 **Increased Incidence of Hepatomas in C3H Mice Peritoneally Inoculated with (C3H x T$_6$)F$_1$ Spleen Cells (Meeting Abstract).** (Eng.) Hard, R. C. (Medical Coll. Virginia, Virginia Commonwealth Univ., Richmond, VA) *Am J Pathol* 86(2): 22a; 1977. (no refs.)

77-3969 **Stress-Related Factors in the Neoplastic Process (Meeting Abstract).** (Eng.) Santisteban, G. A. (Pacific Northwest Res. Foundation, Fred Hutchinson Cancer Res. Center, Seattle, WA 98104) Riley, V.; Spackman, D. *Proc Am Assoc Cancer Res* 18: 172; 1977. (no refs.)

77-3970 **Cancer-Stress Studies: The Effects of Pregnancy on Plasma Corticosterone and Immune System Components in Mice (Meeting Abstract).** (Eng.) Spackman, D. (Pacific Northwest Res. Foundation and Fred Hutchinson Cancer Res. Center, Seattle, WA 98104) Riley, V. *Proc Am Assoc Cancer Res* 18: 172; 1977. (no refs.)

77-3971 **Exocrine Secretion of Immunologically Induced Pancreatic Carcinoma: Persistence of Specificity of Carcinomatous Ascitic Pancreatic Cells.** (Fre.) Thomas, J. A. (Centre de Physiologie Cellulaire, Universite Pierre-et-Marie-Curie, 7, quai Saint-Bernard, 75005 Paris, France) *CR Acad Sci [D] (Paris)* 24(11): 995-1000; 1977.

Daily ip injection of heterologous antilipoprotein induces secretory cell cancer of the exocrine pancreas in CD1 mice. The exocrine secretory specificity is maintained from the adenomatous to the carcinomatous phase, in the evolved carcinoma, and in metastatic and ascitic carcinomatous cells. The latter cease their secretory activity following ip grafting, but in sc graft-induced solid tumors, the secretory activity reappears as confirmed by the presence of trypsinogen and chymotrypsinogen. The inducing immunosera can activate growth in the pancreas and in adipose tissue of the pancreatic ascitic cancers that they themselves induced, and they may occasionally cause nodular hepatic cancers. (6 refs.)

77-3972 **Plasmacytoma After Phenytoin Therapy?** (Ger.) Cohnen, G. (Hamatologische Abteilung, Med. Klinik, Hufelandstrasse 55, D-4300 Essen 1, W. Germany) Heredia, D. M. *Munch Med Wochenschr* 119(9): 309-310; 1977.

The development of a plasmacytoma in a patient who had taken phenytoin for 5 yr for posttraumatic epilepsy and then for another 2 yr after a 2-yr interval is described and discussed in relation to the immunosuppressive properties of phenytoin. (26 refs.)

77-3973 **Acute Myeloblastic Leukemia after Immunosuppressive Treatment.** (Fre.) Bisson, M. (Service de Rhumatologie, Hopital Antoine-Beclere 157, rue de la Porte de Trevaux F 92141 Clamart) Galanaud, P.; Subtil, E. *Nouv Presse Med* 6(22): 1980; 1977.

Three cases of acute myeloblastic leukemia (AML) occurred after treatment of patients with immunosuppressants. One patient was treated with cyclophosphamide for 43 mo, the remaining two with chlorambucil for 14 and 26 mo, respectively. A sideroblastic anemia with thrombopenia appeared 7 mo prior to blastosis in one patient. In another, medullary hypoplasia with partial blastosis, macrocytic anemia, and neutropenia appeared 13 mo before blastosis. In the third case, the first peripheral blood dyscrasias (macrocytic anemia and neutropenia) were noticed $>$ 2 yr after discontinuation of chlorambucil treatment. Bone marrow examined for the first time 1 yr later showed partial blastosis, which was diagnosed as AML; this diagnosis was confirmed on autopsy 28 mo later. Evolution of AML from the onset of the first hematologic signs in these three patients varied from 11 to

26 mo. Comparisons are made with 17 other cases of AML that occurred in patients being treated with immunosuppressants for nonmalignant disorders. (3 refs.)

77-3974 **Alterations in Host Responsiveness in Patients with Prostatic Cancer Following Cryosurgery or Transurethral Resection.** (Eng.) Ablin, R. J. (Div. Immunology, Cook County Hosp., Chicago, IL 60612) Bruns, G. R.; Guinan, P. D.; Sadoughi, N.; Al Sheik, H.; Bush, I. M. *Am Surg* 43(3): 144-150; 1977.

The effect of cryosurgery (CS) or transurethral resection (TUR) on cell-mediated immunologic responsiveness was evaluated in 15 patients (aged 59-84 yr) with prostatic cancer. Five patients had CS, 10 TUR. Proliferative response of the T-cell population of peripheral blood lymphocytes (PBL) following stimulation with phytohemagglutinin (PHA) was used as an in vitro indication of an individual's cellular responsiveness. The five patients receiving CA had a stimulation index [SI: (mean counts/min/10^6 PBL + PHA)/(mean counts/min/10^6 PBL only)] of $<$ 50 before surgery. Afterward, four patients showed a further reduction in SI in autologous serum. The reduction was transient, lasting 2-7 days postsurgery, and the SI then gradually increased to approx twice its preoperative level by 4 wk. In contrast with further reduction in their SI in autologous serum, the SI for PHA-stimulated PBL cultured in homologous serum increased following CS, reaching a plateau after 4-6 wk. Five of TUR patients had an SI in autologous serums of $<$ 50 before surgery. Following TUR, 2/5 had a further decrease in SI, and 5/5 patients with a normal SI before TUR showed a reduction postoperatively. In all, of the 15 patients, 11 had an SI that was less after surgery than before, 2 remained unchanged, and 2 showed an increase in SI. Although transient, depression of lymphocyte proliferation, particularly if it involves tumor-cloned T cells, may provide reduced surveillance to potential metastatic tumor cells, leading to an alteration of tumor-host homeostasis. Pre- and/or postoperative immunotherapy in these patients may be indicated. (27 refs.)

77-3975 **Hodgkin's Disease in Human Renal Transplantation.** (Eng.) Cerilli, J. (Dept. Surgery, Ohio State Univ. Hosps., Columbus, OH 43210) Rynasiewicz, J. J.; Rothermel, W. S. *Am J Surg* 133(2): 182-184; 1977.

Two cases of Hodgkin's disease (HD) in renal allograft recipients are presented, bringing the total number reported in this specific population to three. The cases illustrate the atypical biologic behavior of HD in immunosuppressed patients. The first is of a 23-yr-old woman who underwent bilateral nephrectomy, splenectomy, and related donor renal transplantation. She was maintained on 15 mg prednisone and 125 mg Imuran daily. Five years later she presented for evaluation of diarrhea of 2 yr duration. Barium enema revealed an ulcerating annular nonobstructive lesion in the transverse colon. At laparotomy, two areas of ulceration were found in the resected transverse colon. Microscopic examination revealed HD of mixed cellularity with vascular invasion. The second case is that of a 27-yr-old man who underwent similar surgery and maintenance medication. Seven years after transplantation he presented with hematuria, significant eosinophilia and fever. Liver biopsy contained a nodule composed of eosinophils, Reed-Sternberg cells, and atypical histiocytes. The three known cases indicate that the incidence of HD in renal allograft recipients is 15-30 times greater than that in the normal population. The presence of diarrhea or fever and eosinophilia in a transplant recipient should strongly suggest HD. (13 refs.)

77-3976 **Malignancy After Immunosuppressive Therapy (Letter to Editor).** (Eng.) Mazzei, D. (Cattedra di Immunologia Clinica dell'Universita di Milano, Via Francesco Sforza, 35-20122 Milan, Italy) Polli, E. E.; Quarto di Palo, F. *Boll Ist Sieroter Milan* 56(2): 197; 1977.

Two patients developed neoplasms of the ovary and kidney, respectively, after immunosuppression for transplantation. In addition, a man who received immunosuppressive therapy for dermatomyositis developed bronchial carcinoma. (2 refs.)

77-3977 **Effects of Immunosuppression on the Rejection of Methylcholanthrene Tumor Isografts.** (Eng.) Jacobs, S. C. (Div. Urology, Peter Bent Brigham Hosp., 721 Huntington Ave., Boston, MA 02115) McLaughlin, A. P.; Gittes, R. F. *J Surg Oncol* 9(4): 353-357; 1977.

The effect of immunosuppression with azathioprine (AZA) and/or methylprednisolone (MePR) on primary and secondary immune responses to a transplanted tumor was studied. The ability to reject a methylcholanthrene-induced squamous cell carcinoma of the prostate in Lewis rats was determined by rechallenge with tumor cells after amputation of the primary transplant. Po AZA (20 mg/kg/day) increased the incidence of tumors in a primary challenge, but did not affect the ability of immunized rats to reject subsequent tumor isografts. Similar results were obtained with 2 mg/kg/day ip AZA, 2 mg/kg/day ip MePR, and 2 mg/kg/day ip MePR + 10 mg/kg/day ip AZA. It appears that AZA affects the proliferation of sensitized cells during the immunological response to antigens of this specific tumor. Immunosuppression does not alter the processing of tumor-specific antigens or the cytotoxic effectiveness of the immune system substantially. These data indicate that immunosuppression is safe in transplant patients previously cured of cancer. (6 refs.)

77-3978 **Retarded Growth of Lymphoma in Immunodepressed Mice.** (Eng.) Gillette, R. W. (Cancer Center Hawaii, 1997 East-West Road, Honolulu, HI 96822) Wunderlich, D. A. *J Natl Cancer Inst* 58(4): 1131-1133; 1977.

The growth of YAC and LSTRA lymphomas was studied in normal A/He and BALB/c mice and in nude athymic mice. In most instances, the immunodepressed animals survived longer than their normal counterparts after the iv inoculation of tumor cells. The results were not due to histocompatibility, since increased survival was also observed in animals that had been lethally irradiated and reconstituted with syngeneic bone marrow. The route of injection was critical; when lymphoma cells were inoculated ip, the survival of normal and immunodepressed animals was about the same. (20 refs.)

77-3979 **Prolonged Disease-free Survival in Bronchogenic Carcinoma Associated with HLA-Aw19 and HLA-B5. A Two-Year Prospective Study.** (Eng.) Rogentine, G. N. (Immunology Branch, NCI, Building 10, Room 2N105, 9000 Rockville Pike, Bethesda, MD 20014) Dellon, A. L.; Chretien, P. B. *Cancer* 39(6): 2345-2347; 1977.

Seventy patients with squamous carcinoma or adenocarcinoma of the lung were HLA-typed at time of diagnosis and initial therapy (surgery or radiation). No abnormal HLA-antigen frequencies were found. However, the possession of HLA-Aw19 or HLA-B5 was significantly correlated with 2-yr disease-free survival. Twelve of 21 patients with either Aw19 or B5 were disease-free at 2 yr in contrast to only 6/48 patients lacking either antigen. One patient was lost to follow-up. It is possible that Aw19 and B5 are associated with host resistance to progression of bronchogenic carcinoma. (5 refs.)

77-3980 **Alteration of Friend Virus Induced Erythroleukemia by Active Immunotherapy and Antithymocyte Serum (Meeting Abstract).** (Eng.) Hines, D. L. (Michigan Cancer Foundation, Detroit, MI 48201) Dietz, M.; Furmanski, P.; Rich, M. A. *Proc Am Assoc Cancer Res* 18: 185; 1977. (no refs.)

77-3981 **Anti-tumor Activity of *Listeria Monocytogenes* in Strain 13 Guinea Pigs (Meeting Abstract).** (Eng.) Dustoor, M. M. (Univ. Wisconsin, Madison, WI 53706) Blazkovec, A. A. *Fed Proc* 36(3): 1291; 1977. (no refs.)

77-3982 **Clearance of *Candida Albicans* in Mice Bearing Methylcholanthrene Induced Fibrosarcoma (Meeting Abstract).** (Eng.) Balint, J. P. (Rutgers Univ., New Brunswick, NJ 08903) Tewari, R. P. *Fed Proc* 36(3): 1200; 1977. (no refs.)

77-3983 **Inhibition and Enhancement of Rat Mammary Tumors by Bacillus Calmette-Guerin (BCG) (Meeting Abstract).** (Eng.) Piessens, W. F. (Harvard Medical Sch. and Robert B. Brigham and Peter Bent Brigham Hosps., Boston, MA 02120) Churchill, W. H. *Proc Am Assoc Cancer Res* 18: 170; 1977. (no refs.)

77-3984 **Specific Simian Virus 40 (SV40)-induced Immunity Against Transplantable SV40 Tumor in Syrian Hamsters: Abrogation by BCG Vaccination.** (Eng.) Zhalgasbayeva, G. T. (Lab. Tumor Immunology, Cancer Res. Center, Acad. Medical Sciences, Moscow 115 478, Kashirskoye Shosse 6, USSR) Deichman, G. I. *J Natl Cancer Inst* 58(4): 1121-1124; 1977.

Syrian hamsters were immunized id with simian virus 40 (SV40, $10^{7.2}$-$10^{7.5}$ median tissue culture infective dose/1.0 ml) and/or BCG (0.25 mg) in different time and sequence combinations) and then subsequently challenged with SV40-induced transplantable tumor cells. Immunization of hamsters with some but not all BCG preparations alone induced high levels of resistance to SV40 transplantable tumor cells. SV40 immunization of hamsters previously inoculated with BCG induced antitumor immunity equal the resistance induced by immunization of normal animals with SV40. No cumulative effects of BCG and SV40 immunizations were noticed, even when BCG preparations alone induced a considerable increase of antitumor resistance. Inoculation of animals with a mixture of SV40 and BCG was generally less effective than that with SV40 alone. Inoculation of BCG preparations into hamsters preimmunized with SV40 resulted in complete or partial abrogation of the resistance induced by SV40. All BCG preparations, independently of their antitumor activity per se, decreased the resistance induced by SV40. The effect of this BCG-induced abrogation of resistance was observed in animals immunized with SV40 7-427 days before BCG inoculation. The effect was still observed 3 mo after BCG inoculation. (13 refs.)

77-3985 **Potential for Immunization Against Herpesvirus-Induced Oncogenesis with Plasma Membrane Vesicles (Meeting Abstract).** (Eng.) Scott, R. E. (Mayo Clinic/Foundation, Rochester, MN) Pearson, G. R. *Am J Pathol* 86(2): 27a; 1977. (1 ref.)

77-3986 **Syngeneic Tumor Rejection Induced by Immunization with Normal Allogeneic Tissues.** (Eng.) Bear, R. H. (Dept. Immunology Res., Roswell Park Memorial Inst., Buffalo, NY 14263) Roholt, O. A.; Pressman, D. *Immunol Commun* 6(3): 217-225; 1977.

Immunization of normal allogeneic kidney and liver tissue prolonged the survival of DBA/2Cr mice challenged with a lethal dose of syngeneic L5178Y lymphoma cells. A cross-reaction between tumor-associated transplantation antigens and non-H-2 alloantigens may provide this protection. (16 refs.)

77-3987 **SV40 Tumor Rejection Induced by Vesicular Stomatitis Virus Bearing SV40 Tumor-specific Transplantation Antigen (SV40-TSTA). I. Specificity of Immunoprotection and Effect of Enzyme on TSTA Activity.** (Eng.) Ansel, S. (Institut de Recherches Scientifiques sur le Cancer, B.P. No. 8, 94800 Villejuif, France) Huet, C.; Tournier, P. *Int J Cancer* 20(1): 51-60; 1977.

The simian virus 40 tumor-specific transplantation antigen (SV40-TSTA) specificity of tumor rejection was studied with highly purified vesicular stomatitis virus (VSV) from VSV-infected SV40-transformed hamster cell lines. Immunization with this virus protected hamsters against challenge with SV40-transformed cells (TSV$_5$-cl$_2$). This protection was obtained regardless of the source of the SV40-transformed cells (cat, rat, or hamster) used to produce VSV and was, therefore, associated with SV40-TSTA. Furthermore, when grown on spontaneously transformed cell lines or on cells transformed by a different oncogenic DNA virus, such as polyoma virus, VSV failed to protect against the SV40-induced tumor. It was concluded that the SV40-TSTA activity of purified VSV is due to the incorporation of SV40-TSTA within the viral envelope. When VSV was treated with proteolytic enzymes (bromelain, trypsin), no loss of TSTA-induced tumor rejection was observed, although VSV had lost its ability to induce virus-neutralizing antibody. This demonstrates that TSTA activity is not related to the viral spikes. Phospholipase C suppressed TSTA activity, but neutralizing activity was still detectable in the anti-VSV sera. The results demonstrate that the protection afforded by VSV is highly specific and suggest that SV40-TSTA activity may be conveyed by the lipid core of the viral envelope. (38 refs.)

77-3988 **SV40 Tumor Rejection Induced by Vesicular Stomatitis Virus Bearing SV40 Tumor-specific Transplantation Antigen (SV40-TSTA). II. Association of SV40-TSTA Activity with Liposomes Containing VSV Glycolipids.** (Eng.) Huet, C. (Institut de Recherches Scientifiques sur le Cancer, B.P. No. 8, 94800 Villejuif, France) Ansel, S. *Int J Cancer* 20(1): 61-66; 1977.

Highly purified vesicular stomatitis virus (VSV) was obtained from VSV-infected, simian virus 40 (SV40)-transformed and normal hamster cell lines. A glycolipid extract was prepared from these VSV preparations according to the Folch partition procedure. These glycolipids were rendered immunogenic to Syrian hamsters when incorporated within liposomal membranes composed of lecithin/sphingomyelin/cholesterol (1/1/2 by wt). When the glycolipids were extracted from VSV grown on cell lines (TSV$_5$-cl$_2$ and EHSVi-cl$_1$) that contained the SV40 tumor-specific transplantation antigen (SV40-TSTA), it was possible either to induce tumor rejection or at least to slow the growth of the tumor in Syrian hamsters challenged with TSV$_5$-cl$_2$ cells. No protection was obtained in animals treated with liposomes containing glycolipids extracted from purified VSV grown on SV40-TSTA-negative cells (EHB). The SV40-TSTA could be a glycolipid of the transformed cell membrane that is incorporated within the VSV envelope. (29 refs.)

77-3989 **Specific Immune Response Against Syngeneic SV-40 Tumor Associated Antigens in Mice (Meeting Abstract).** (Eng.) Glaser, M. (NCI, NIH, Bethesda, MD 20014) Law, L. W. *Proc Am Assoc Cancer Res* 18: 237; 1977. (no refs.)

77-3990 **Migration Inhibition by an Agarose Microdroplet Assay: Monitoring of Tumor-associated Antigens on a Simian Virus 40-induced Sarcoma.** (Eng.) McCoy, J. L. (Lab. Immunodiagnosis, NCI, Bethesda, MD 20014) Padarathsingh, M.; Dean, J. H.; Henriksen, O.; Natori, T.; Law, L. W. *J Immunol* 119(1): 306-310; 1977.

Macrophage migration inhibition assays, with a direct agarose microdroplet method, were used to monitor the tumor-associated antigen (TAA) activity of preparations of simian virus 40 (SV40)-induced mKSA cells of BALB/c mice. These preparations included cell-free crude membranes and papain-solubilized and NP40 detergent-solubilized membrane extracts from MKSA tumor cells. The assay was extremely sensitive; it could detect migration inhibition reactivity with all three types of antigenic preparations with concentrations as low as 250 picograms protein/ml. The reactivities were reproducible in repeat experiments with the same or different lots of the antigen preparations. The reactivities were specific in that peritoneal exudate cells from BALB/c mice, immunized with antigenically unrelated but syngeneic plasmacytomas, were not inhibited by the antigens. The results demonstrate the usefulness of this assay in rapidly detecting small concentrations of partially purified TAA preparations by employing a small number of immune cells. (18 refs.)

77-3991 **Tumor Associated Antigens (TAA) in the Cytosol and Plasma Membranes of Rat Moloney**

Sarcoma Cells (MST-1) (Meeting Abstract). (Eng.) Leung, K. (Scripps Clinic and Res. Foundation, La Jolla, CA 92037) Feldman, J. D. *Fed Proc* 36(3): 1260; 1977. (no refs.)

77-3992 **Carcinoneonatal Antigens on SV40 Transformed Syngeneic Cells (Meeting Abstract).** (Eng.) Abramson, C. (Pennsylania Coll. Podiatric Medicine, Philadelphia, PA 19107) Axler, D.; Hetherington, V.; Kavros, S. *Fed Proc* 36(3): 1260; 1977. (no refs.)

77-3993 **Assessment of Common Target Antigens on EBV Transformed Lymphocytes and Fresh Human Acute Leukemia Cells (Meeting Abstract).** (Eng.) Zarling, J. M. (Univ. Wisconsin, Madison, WI 53706) Bach, F. H. *Proc Am Assoc Cancer Res* 18: 249; 1977. (no refs.)

77-3994 **In Vivo-In Vitro Modulation of Viral Antigens of Lymphoma Cells (Meeting Abstract).** (Eng.) Sabbath, M. (Depts. Pathology, Lenox Hill Hosp., New York, NY 10021) Pearse, A.; Ioachim, H. L. *Proc Am Assoc Cancer Res* 18: 183; 1977. (no refs.)

77-3995 **New Antigens of the Tumor Cell Surface.** (Ger.) Ignjatovic, J. (Inst. Application Nuclear Energy in Agriculture, Veterinary Medicine, and Forestry, Zemun, Yugoslavia) *Umschau Wiss Tech* 77(11): 350-351; 1977.

Cellular cytotoxicity assays with avian cells show that virally (avian sarcoma virus) or chemically transformed cells have at least one cell surface antigen in common, but that the virally transformed cells have a further antigen complex specific for the virus. (1 ref.)

77-3996 **Cell Surface Antigens of Spontaneously Metastasizing and Nonmetastasizing Mammary Tumors (MT) in Rats (Meeting Abstract).** (Eng.) Kim, U. (Roswell Park Memorial Inst., Buffalo, NY 14263) Yamamoto, M. *Proc Am Assoc Cancer Res* 18: 204; 1977. (no refs.)

77-3997 **Similar Cell Surface Antigens on Hamster Cells Transformed by Different Papovaviruses.** (Eng.) Molinaro, G. A. (Dept. Microbiology, Univ. Illinois at Medical Center, Chicago, IL 60680) Major, E. O.; Bernhardt, G.; Dray, S.; di Mayorca, G. *J Immunol* 118(6): 2295-2298; 1977.

Baby hamster kidney cells (BHK) transformed by 1/3 papovaviruses, simian virus 40 (SV40), rodent polyoma, or human BK virus, were tested for surface antigens by an immunocytoadhesion method. The cells were sensitized with rabbit antisera to cell clones transformed by polyoma or BK virus and then rosetted with RBC coated with antibody to rabbit immunoglobulin. These antisera detected common antigens on BHK cells transformed by any of the three papovaviruses, but apparently not on normal BHK cells. These antigens do not appear to be associated solely with transformation, because they were not significantly expressed on BHK cells that were transformed chemically, spontaneously, or by an oncornavirus. Immunocytoadhesion might be able to distinguish virus-related cell surface antigens from embryonal antigens and from transplantation antigens. (16 refs.)

77-3998 **Light and Electron Microscopy of Mouse Mammary Epithelial Cells Labeled for Mammary Tumor Virus and Other Antigens (Meeting Abstract).** (Eng.) Nemanic, M. K. (Univ. California, Berkeley, CA 94720) *Diss Abstr Int [B]* 37(9): 4358; 1977. (no refs.)

77-3999 **Soluble TSTA of a Chemically Induced Sarcoma (Meeting Abstract).** (Eng.) Natori, T. (NCI, NIH, Bethesda, MD 20014) Law, L. W.; Appella, E. *Proc Am Assoc Cancer Res* 18: 237; 1977. (no refs.)

77-4000 **Antigenic Differences Between Primary Methylcholanthrene-induced Rat Sarcomas and Post-surgical Recurrences.** (Eng.) Pimm, M. V. (Cancer Res. Campaign Labs., Univ. Nottingham, Univ. Park, Nottingham NG7 2RD, England) Baldwin, R. W. *Int J Cancer* 20(1): 37-43; 1977.

The immunogenicities of in vivo lines established from primary methylcholanthrene (MC)-induced rat sarcomas were compared with those of lines initiated from tumor recurrences at the excision site of the primaries. Lines from two of four primary sarcomas showed little or no immunogenicity, as assessed by protection against challenge afforded by graft excision or implantation of irradiated tissue. In contrast, lines from all four recurrences were immunogenic, giving protection against up to 5 x 10^6 tumor cells. Most importantly, with all four tumors, lines established from recurrences were antigenically distinct from lines derived from their primary sarcomas, so that immunization with regrowth lines gave no protection against lines from the primaries, and vice versa. The fact that primary MC-induced sarcomas are antigenically distinct from recurrent tumors implies that they arose by clonal amplification of separate populations of transformed cells. This may reflect proliferation of dormant neoplastic cells or the further induction of transformed cells by residual carcinogen. These findings are relevant to the multifocal origin of tumors and for the design of active immunotherapy for treating recurrences or metastatic deposits. (21 refs.)

77-4001 **Molecular Similarities Between the Qa-2 Alloantigen and Other Gene Products of the 17th Chromosome of the Mouse.** (Eng.) Michaelson, J. (Memorial Sloan-Kettering Inst. Cancer Res., New York, NY 10021) Flaherty, L.; Vitetta, E.; Poulik, M. D. *J Exp Med* 145(4): 1066-1070; 1977.

The *Qa-2* region of the 17th chromosome of the mouse contains two previously unrecognized genes, one that codes for an antigen on thymus, spleen, and lymph node, and one that is expressed on spleen and lymph node only. These gene products were examined biochemically. The following sera were used: rabbit anti-mouse immunoglobulin (Ig), goat anti-mouse Ig, goat anti-rabbit Ig, αKb, αDb, αQa-2, and αβ2M. Using αQa-2 to precipitate antigens from Qa-2+ lymph node cells (LNC) of C57Bl/6, HTH, or B6.K2 mice, two proteins with apparent molecular wts of approx 43,000 and 12,000 daltons were resolved on 7.5% and 10% acrylamide gels. The precipitate contained approx 0.15% of the total labeled protein. Immunoprecipitates from lysates of spleen cells also showed these peaks, but in half the quantity of Qa-2 found on LNC. No Qa-2 was found on thymocytes. The reaction of αQa-2 serum with thymocytes in the cytotoxicity assay is probably due to a second antigen specified by the Qa-2 region. The amounts of Qa-2 recovered from thymus, spleen, and LNC paralleled the number of mature T cells found in these organs. LNC from Qa-2- mice (B6-*H-2k* or B6.K1) did not yield peaks with αQa-2. Since B6.K1 and B6.K2 mice are genetically identical except for a small portion of the 17th chromosome adjacent to Qa-2, the peaks detected can be ascribed to the Qa-2 antigen found on LNC in the cytotoxicity assay. Sequential precipitation demonstrated that Qa-2 is distinct from H-2D and H-2K molecules. The molecular similarity between H-2D, H-2K, TL, and Qa-2 is remarkable in that they are all molecules of approx 45,000 daltons associated with a small subunit that can be serologically identified as β2-microglobulin. (18 refs.)

77-4002 **Tumor Antigen and Human Chorionic Gonadotropin in CaSki Cells: A New Epidermoid Cervical Cancer Cell Line.** (Eng.) Pattillo, R. A. (Dept. Gynecology and Obstetrics, Medical Coll. Wisconsin, Milwaukee, WI 53226) Hussa, R. O.; Story, M. T.; Ruckert, A. C.; Shalaby, M. R.; Mattingly, R. F. *Science* 196(4297): 1456-1458; 1977.

The establishment of the CaSki cell line from an epidermoid carcinoma of the human cervix is reported. Tumor-associated antigen was recovered from the medium in which these cells were grown. Leukocytes from 17 cervical cancer patients, 17 normal donors, and 11 patients with other types of cancer were tested with the CaSki tumor-associated antigen in the direct leukocyte migration inhibition (LMI) assay. LMI was observed in 76.5% of the cervical cancer patients, 17.6% of the normal donors, and 27.3% of the patients with other types of cancer. Analysis of the serum from the donor of the cell line at the time of tumor biopsy and of CaSki culture fluids by double radioimmunoassay demonstrated the presence of the β subunit of human chorionic gonadotropin. The presence of this hormone in the cells in culture > 1 1/2 yr later gives evidence of the apparent irreversibility of the depression that occurred in the production by cervical carcinoma cells of this placental hormone marker. (14 refs.)

77-4003 **Xenogenic Antisera to Tumor-associated Antigen of Ovarian Carcinoma (Meeting Abstract).** (Eng.) Gerber, M. A. (Mount Sinai Sch. Medicine, City Univ. New York, New York, NY) Faiferman, I.; Cohen, C. J.; Koffler, D. *Am J Pathol* 86(2): 78a-79a; 1977. (no refs.)

77-4004 **Inhibition of Proliferative and Plaque-forming Cell Responses by Human Bone-Marrow-derived Lymphocytes from Peripheral Blood by Antisera to the p23,30 Antigen.** (Eng.) Friedman, S. M. (Div. Tumor Immunology, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA 02115) Breard, J. M.; Humphreys, R. E.; Strominger, J. L.; Schlossman, S. F.; Chess, L. *Proc Natl Acad Sci USA* 74(2): 711-715; 1977.

A technique for the polyclonal induction of plaque-forming cells from human peripheral blood B lymphocytes was used to assess the role of a human Ia-like antigen (p23,30) in the differentiation of B cells. In particular, the effects of antisera to p23,30 on the plaque-forming cells and the proliferative responses of human B cells stimulated by pokeweed mitogen (PWM) or soluble products of activated human T lymphocytes were examined. Antisera to p23,30 eliminated the development of plaque-forming cells induced by both T-cell products and PWM. Although antisera also abrogated B-cell proliferation induced by T-cell supernatants, the proliferative response generated by PWM was only partially reduced. The p23,30 antigen continued to be expressed on fully differentiated plaque-forming cells, but antisera to this determinant inhibited B-cell differentiation only when present during the early stages of B-cell cultures. These results lend further support to the analogy between p23,30 and murine Ia antigens. Moreover, they demonstrate a major role for this antigen in the early events involved in the differentiation of B cells into antibody-forming cells. (18 refs.)

77-4005 **The Appearance of Non-specific Antibody-forming Cells in the Efferent Lymph Draining Antigen-stimulated Single Lymph Nodes.** (Eng.) Poskitt, D. C. (Basel Inst. Immunology, Grenzacherstrasse 487, Postfach 4005, Basel 5, Switzerland) Frost, H.; Cahill, R. N.; Trnka, Z. *Immunology* 33(1): 81-89; 1977.

The synthesis and secretion of specific antibody and non-specific immunoglobulins were investigated. The immune response to an antigen stimulated the maturation of lymphocytes whose specificities were not related to that of the injected immunogen. This mechanism may be important in maintaining imunological memmory. (35 refs.)

77-4006 **A Comparison of Antibody Responses to EBV-Associated Antigens in Nasopharyngeal Carcinoma Patients from North America, Tunisia, France and Hong Kong (Meeting Abstract).** (Eng.) Wallen, W. C. (NIH, Bethesda, MD 20014) Levine, P. H.; Granlund, D. A.; Ablashi, D. V.; Connelly, R. *Proc Am Assoc Cancer Res* 18: 201; 1977. (no refs.)

77-4007 **Antibody to Epstein-Barr Virus in Sera from Children with Various Neoplasias.** (Rus.) Gurtsevich, V. E. (Inst. Experimental and Clinical Oncology, Acad. Medical Sciences USSR, Moscow, USSR) Stepina, V. N.; Iarymova, N. M.; Ermakov, E. S.; Mazurenko, N. P.; Durnov, L. A. *Vopr Virusol* (6): 663-668; 1976.

Using immunofluorescence, an attempt was made to determine the relationship between antibodies to Epstein-Barr virus (EBV) and common neoplasias in children. Eighty-one sera from healthy children and from adults were used for controls. A suspension culture of P3Hr-1 cells, a clone of the P3Jx strain of Burkitt's lymphoma, was used for testing. Assuming that the amount of EBV antibodies depended on the age of children, the control group was divided into Groups A (10 children, ages 4-7 yr) and B (18 children, ages 8-14 yr), whose geometric mean antibody titer was 1:86 and 1:58, respectively. For the adult donors, it was 1:47. There was no increase in the amount of antibodies to EBV compared with controls. Because of the age differences among the groups, the geometric mean antibody titer of soft tissue sarcoma (1:80) was compared to the mean for Group B children (1:58), and Group A children (1:86) served as the controls for patients with neuroblastoma (1:09) and reticulum cell sarcoma (1:93). The amount of antibodies decreased in 18 children with Wilms' tumor (1:51) and in 6 with teratoblastoma (1:26), compared to Group A (1:86). Sera from 21 children with benign tumors showed the same antibody titer as those of Group B. The authors concluded that the amount of antibodies to EBV in children with neoplasia is approx the same as that in healthy children. The level depends on age. It was also found that the incidence of EBV infection in various groups of sick and healthy children varied from 82% to 100%. (6 refs.)

77-4008 **Relation Between Primary Cancer of the Liver and Australia Antigen or Anti-Australia Antibody HB in Greece.** (Fre.) Theodoropoulos, G. (Service de Physiologie Pathologique, Faculte de Medicine d'Athenes, Athenes -609, Greece) Economopoulos, P.; Archimandritis, A.; Mellissinos, K. *Nouv Presse Med* 6(8): 654; 1977.

Primary cancer of the liver (PCL) and its reputed relation to serum Australia antigen (hepatic B surface antigen, HBsAg) are discussed. The frequency of PCL is greater in Greece than in the rest of Europe, and it has been suggested that there are high serum levels of HBsAg in PCL patients. However, results obtained by the authors do not support that contention. HBsAg serum levels were determined radioimmunologically and the corresponding antibody (anti-HBsab) levels by hemagglutination. The frequency of HBsAg and anti-HBsab was the same in patients with PCL plus cirrhosis and in patients with cirrhosis alone. A genetic predisposition to PCL in Greece cannot be excluded. (8 refs.)

77-4009 **Production of Antibodies Against Influenza Virus by Somatic Cell Hybrids Between Mouse Myeloma and Primed Spleen Cells.** (Eng.) Koprowski, H. (Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA 19104) Gerhard, W.; Croce, C. M. *Proc Natl Acad Sci USA* 74(7): 2985-2988; 1977.

A somatic cell hybrid was produced between spleen cells from a BALB/c mouse immunized with purified influenza virus and mouse myeloma cells. Antibodies specific for the hemagglutinin of the virus were produced in large quantities. When these hybrids were injected sc into BALB/c mice, tumors developed at the site of inoculation. (16 refs.)

77-4010 **Natural Antibody in Mammary Tumor Virus-infected Mice That Reacts with Intracytoplasmic A Particles of Mouse Mammary Tumors.** (Eng.) Zotter, S. (Inst. Pathology, Medical Acad. "Carl Gustav Carus," Fetscherstrasse 74, 8019 Dresden, E. Germany) Muller, M. *J Natl Cancer Inst* 58(4): 967-975; 1977.

By an indirect immunofluorescence technique with prolonged serum incubation of murine mammary tumor (MT) slices, 179/424 mice were found to possess natural serum antibody that reacted with intracytoplasmic A particles (iAp) of MT cells. The immunologic specificity of this antibody was supported by absorption and blocking experiments. Furthermore, there was a strong similarity between the mouse antibody reaction on various MT and the fluorescence pattern of rabbit anti-iAp antiserum on these tumors. In female mice, antibody incidence and geometric mean titers were correlated with the spontaneous MT frequency of the mouse strains examined. Some XVII/Bln and CBA/BlnfXVII/Bln mice also contained anti-iAp antibody in their sera, although these strains are supposedly free of mouse mammary tumor virus (MuMTV). In contrast to MuMTV-producing CBA/Bln mice, these animals did not possess detectable spontaneous antibody reacting with MuMTV-B particles. Therefore, the antibody response in these mice might be induced by incomplete MuMTV expression. CBA/Bln females ≥ 4 mo had significantly higher antibody titers than 4-wk-old females. A history of lactation did not influence antibody levels. In the comparatively high MT strains CBA/Bln and C3H/Bln, adult (4-mo-old) females had significantly higher antibody levels than age-matched males. (42 refs.)

77-4011 **Antibody Synthesis Stimulation by Vitamin A in Chickens.** (Eng.) Leutskaya, Z. K. (Lab. Helminthology, Acad. Sciences USSR, Moscow, USSR) Fais, D. *Biochim Biophys Acta* 475(2): 207-216; 1977.

The effect of vitamin A on the immune response of white Leghorn chickens was studied. Following primary ip immunization with 1 ml of human serum albumin or *Ascaridia galli*, the antibody content of the chicken sera depended on the dose of vitamin A in the diet. In chickens fed a high dose of vitamin A (4,000 IU/day), the serum antibody level was two to five times as high as the level in chickens that had not been given vitamin A. An additional dose of vitamin A administered po any day following reimmunization increased the antibody content; the effect was most pronounced when vitamin A was given on the third day after reimmunization. In the period of max antibody synthesis (fourth day after reimmunization), incorporation of labeled retinol was 13 times higher in the spleens of reimmunized chickens than in the spleen of control chickens. In vitro studies of antibody synthesis by spleen cells demonstrated that addition of retinyl palmitate to the incubation medium enhanced antibody synthesis. Addition of retinyl palmitate to the spleen cells of vitamin A-deficient chickens restored the synthesis to the control level. The possibility that the effect of vitamin A on the immune process is realized at the level of immunoglobulin synthesis is discussed. (29 refs.)

77-4012 **Antibody Stimulation of Tumor Cells.** (Eng.) Ryan, W. L. (Dept. Biochemistry, Univ. Nebraska Medical Center, 42nd and Dewey, Omaha, NB 68105) Durick, M. A. *Proc Soc Exp Biol Med* 155(3): 420-423; 1977.

The γ globulin fraction of antiserum to normal dog kidney cells stimulated cell division in a transformed dog kidney cell line. It is suggested that the antibody to normal tissue that appears after injury is responsible for tumor promotion by tissue damage. (22 refs.)

77-4013 **Epstein-Barr Herpesvirus Infection: Inhibition by Immunologically Induced Mediators with Interferon-like Properties.** (Eng.) Lai, P. K. (Clinical Studies Unit, Lab. Viral Carcinogenesis, NCI, NIH, Bethesda, MD 20014) Alpers, M. P.; MacKay-Scollay, E. M. *Int J Cancer* 20(1): 21-29; 1977.

When sensitized WBC from Epstein-Barr virus (EBV)-seropositive adults were reexposed to EBV antigen or to tuberculin-purified protein derivatives, they produced lymphokines. These lymphokines included migration inhibition factor, which inhibits the migration of guinea-pig peritoneal exudate cells, and other lymphokines with the characteristics of interferon, which inhibit EBV-induced transformation and EBV superinfection of target cells. Unsensitized WBC from seronegative adults and from neonates did not produce lymphokines when challenged with the antigens. This indicates that cell-mediated immunity and its associated soluble mediators may be involved in the control of EBV infection and that the interferon release assay is a useful in vitro correlate for the study of cellular immunity to EBV. (31 refs.)

77-4014 **Suppression of In Vitro Epstein-Barr Virus Infection. A New Role for Adult Human T Lymphocytes.** (Eng.) Thorley-Lawson, D. A. (Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA 02115) Chess, L.; Strominger, J. L. *J Exp Med* 146(2): 495-508; 1977.

Studies with Epstein-Barr virus indicated that unfractionated adult lymphocytes transformed less efficiently than fetal cord lymphocytes owing to adult T-cell suppression of B-cell proliferation. This suppression mechanism could play a role in recovery from an Epstein-Barr virus infection. (35 refs.)

77-4015 **Suppressor Cell Regulation of Immune Response to Tumors: Abrogation by Adult Thymectomy.** (Eng.) Reinisch, C. L. (Div. Tumor Immunology, Sidney Farber Cancer Inst., Dept. Medicine, Harvard Medical Sch., Boston, MA 02115) Andrew, S. L.; Schlossman, S. F. *Proc Natl Acad Sci USA* 74(7): 2989-2992; 1977.

The role of the adult thymus in the generation of splenic suppressor T cells by adjuvant was investigated. It appears that the adult thymus regulates the immune responsiveness by exporting suppressor T cells to peripheral lymphoid tissue.

These cells regulate responses to allogeneic and tumor antigens. (23 refs.)

77-4016 **Involvement of T Cells in the Recall of Salmonella-induced Resistance to Tumour.** (Eng.) Ashley, M. P. (Dept. Microbiology and Immunology, Univ. Adelaide, South Australia 5000, Australia) Kotlarski, I.; Hardy, D. *Immunology* 32(1): 1-10; 1977.

When mice are immunized with *Salmonella enteritidis* 11RX (11RX) they develop resistance to tumor growth. The degree and duration of resistance are dependent on the routes of immunization and tumor challenge. When tumor growth resistance declines, it can be recalled using various 11RX antigen preparations. The ability to recall resistance to ip challenge with ^{131}I-labeled Ehrlich ascites tumor cells was transferred to normal (C57BL/6J male and BALB/cJ female) F_1 hybrid mice by ip injection of an antigen preparation of 11RX mixed with spleen cells from 11RX -immunized mice. Apparently, the active cells in this test were sensitized T cells, since spleen cells from normal mice were not effective and the activity of immune spleen cells was markedly reduced by removing θ-antigen-bearing cells but not by removing glass-adherent cells. The induction of in vivo cytotoxicity appeared to depend on the involvement of radiation-sensitive cells derived from nonimmunized recipients, because recall of resistance to tumor challenge was reduced when irradiated mice were used as recipients of spleen cells from immunized mice. (25 refs.)

77-4017 **Thymus Origin of Acute Lymphatic Leukemia and of Non-Hodgkin's Lymphoma in Childhood.** (Ger.) Zintl, F. (Kinderklinik des Bereichs Medizin der Friedrich-Schiller-Universitat Jena, Jena, E. Germany) Plenert, W. *Dtsch Gesundheitsw* 31(52): 2465-2471; 1977.

Leukemia cells from 20 children with acute lymphatic leukemia (ALL) and lymphoma cells from 3 children with lymphosarcoma (LS) were examined for T- and B-lymphocyte markers on their cell membranes. Spontaneous rosette formation (E rosettes) with sheep RBC and reaction with antithymocyte serum served as T-cell markers, and the presence of surface immunoglobulins served as a B-cell marker. The leukemia cells of five ALL children with mediastinal tumors formed E rosettes and reacted with the antithymocyte serum. Fourteen ALL patients did not show this reaction; in addition, their cells lacked surface immunoglobulins. Two of the three LS children were E rosette-positive. The lymphomas originated in the mediastinum and in Waldeyer's ring. There was a good correlation between E rosette formation and reaction with antithymocyte serum. After absorption with peripheral WBC, antithymocyte serum reacted with E-positive lymphoblasts but not with normal peripheral T-lymphocytes. Consequently, leukemia cells that are E rosette-positive possess a T lymphocyte-associated antigen and a thymus-associated antigen. Moreover, these lymphoblasts show a focal acid phosphatase reaction. (30 refs.)

77-4018 **Cell Surface Modification of Dunning Leukemia Cells: Relationship to Virulence (Meeting Abstract).** (Eng.) Assaker, B. (Boston Coll., Chestnut Hill, MA 02167) Rule, A. H.; Miller, H. *Fed Proc* 36(3): 1243; 1977. (no refs.)

77-4019 **Ultrastructure of In Vitro Lymphocyte Transformation After Stimulation with Phytohemagglutinin and Levamisole.** (Spa.) Forteza Vila, J. (Servicio de Anatomia Patologica, Cuidad Sanitaria "Juan Canalejo," La Coruna, Spain) Goyanes-Villaescusa, V. *Sangre (Barc)* 22(2): 164-168; 1977.

Levamisole, when added to phytohemagglutinin, enhanced in vitro lymphocyte transformation. However, this enhancement was not accompanied by ultrastructural changes in the transformed lymphocytes. The morphology of the transformed lymphocytes was thus similar to that found after stimulation with phytohemagglutinin and consistent with that expected in transformed T lymphocytes. (21 refs.)

77-4020 **Control Mechanism of Lymphocyte Traffic: A Study of the Action of Two Sulfated Polysaccharides on the Distribution of ^{51}Cr-[^{3}H]Adenosine-labeled Mouse Lymph Node Cells.** (Eng.) Freitas, A. A. (Lab. Cell Ecology, Sloan-Kettering Inst. Cancer Res., New York, NY 10021) de Sousa, M. *Cell Immunol* 31: 62-76; 1977.

The effects of dextrans of varying molecular wts and of pentosan sulfate (PS) on the distribution of ^{51}Cr-labeled BALB/c mouse lymph node cells were studied in vivo, ie, in recipients treated with the sulfated polysaccharides, and in vitro, ie, by following the fate of cells treated in vitro in intact syngeneic recipients. Both types of experiments demonstrated that dextrans, especially dextran sulfate (DXS) and PS, considerably reduce lymph node entry of the lymphocytes, with concomitant increases in the blood and, in the case of DXS, in the blood and lungs. A parallel quantitative autoradiographic analysis of the distribution of ^{3}H-adenosine-labeled cells confirmed the data with the ^{51}Cr-labeled cells. In addition, it indicated that DXS and PS slow down the circulation of lymphocytes through the marginal zone and red pulp of the spleen and, in the case of DXS, through the pulmonary capillary bed. Unusually large numbers of unlabeled lymphocytes were found in the endothelial wall of the postcapillary venules in the lymph nodes of PS-treated mice. (30 refs.)

77-4021 **Characteristics of BALB/c T Cell Lymphomas as Continuous In Vitro Line (Meeting Abstract).** (Eng.) Kim, K. J. (NIH, Bethesda, MD 20014) Mathieson, B. J.; McKeer, P. E.; Asofsky, R. *Fed Proc* 36(3): 5220; 1977. (no refs.)

77-4022 **Detection, Purification and Functional Characterization of a SIg Negative Human Lymphocyte Subpopulation (Meeting Abstract).** (Eng.) Papermaster, V. M. (Dept. Surgery, Univ. Texas Medical Branch, Galveston, TX) Denis, K. A.; Harris, N. S. *Fed Proc* 36(3): 1314; 1977. (no refs.)

77-4023 **Immunoglobulin-like Messenger RNA in a Mouse T Cell Lymphoma.** (Eng.) Rabbitts, T. H. (MRC Lab. Molecular Biology, Hills Road, Cambridge CB2 2QH, England) Forster, A.; Smith, M.; Gillam, S. *Eur J Immunol* 7(1): 43-48; 1977.

RNA-driven complementary DNA (cDNA) hybridization experiments were carried out to detect complementary sequences in RNA prepared from a mouse T-cell-lymphoma line (EL4). In 0.1 M phosphate buffer, in which light (L)-chain cDNA hybridized efficiently with homologous P3 myeloma messenger RNA (mRNA), poor hybridization was observed with EL4 mRNA unless a low criterion of hybrid formation was used (ie, hydroxyapatite fractionation). The hybrid formed between EL4 mRNA and L-chain cDNA had a melting point 5 C lower than the homologous hybrid, indicating that the sequence detected in EL4 mRNA was similar to but not identical with the P3 mRNA sequence. This gene product may not be confined to T cells, since a similar sequence was detected in a Cλ-producing myeloma cell line. (48 refs.)

77-4024 **Presence in Immunostimulated Cells of an RNA Usable as a Matrix for the Reverse Transcriptase of Avian Myeloblastosis Virus (AMV).** (Fre.) Kayibanda, B. (Institut de Cancerologie et d'Immunogenetique, Hopital Paul-Brousse, 14, av. Paul-Vaillant-Couturier, 94800 Villejuif, France) Fossar, N.; Huppert, J. *CR Acad Sci [D] (Paris)* 284(2): 147-149; 1977.

Cytoplasmic RNA extracted from antigen-stimulated immunocompetent spleen cells and T lymphocytes of CBA mice was transcribed into DNA by the RNA-directed DNA polymerase (reverse transcriptase) from avian myeloblastosis virus, in the absence of added primer. Cytoplasmic RNA from other organs of the same animal, from nonstimulated immunocompetent cells, or from cells in tissue culture was not transcribed in the absence of exogenous primer. (10 refs.)

77-4025 **Characterization of Circulating Immune Complexes in Rats with a Gross Virus Induced Lymphoma (Meeting Abstract).** (Eng.) Begent, R. (Imperial Cancer Res. Fund Lab., P. O. Box 123, Lond WC2A 3PX) Tucker, D. F. *Proc Am Assoc Cancer Res* 18: 184; 1977. (no refs.)

77-4026 **Macrophages Isolated from Regressing Moloney Sarcomas Are More Cytotoxic Than Those Recovered from Progressing Sarcomas.** (Eng.) Russell, S. W. (Dept. Immunopathology, Scripps Clinic and Res. Foundation, La Jolla, CA 92037) McIntosh, A. T. *Nature* 268(5615): 69-71; 1977.

Macrophages were isolated 7-13 days after inoculation from either regressing or progressing Moloney sarcomas (MSC) induced in 6- to 8-wk-old male BALB/c mice by im injection of either 5×10^3 or 10^6 cultured MSC cells, respectively. As measured by in vitro release of ^{51}Cr at a density of 1,500 mm^{-2}, macrophages recovered from regressing tumors killed both P815 mastocytoma and simian virus 40-transformed 3T3 target cells with different efficiencies (probably reflecting differences in susceptibility). However, neither target cell was affected by macrophages collected from progressors. In experiments using a series of monolayers of increasing macrophage density ($0.5\text{-}3.0 \times 10^{-3}$ mm^{-2}), progressor macrophages exhibited a capacity to kill, but their relative cytotoxicity was much less than that of regressor macrophages. This diminished cytotoxicity may be due to inadequate activation of these cells by intratumoral lymphocytes. (13 refs.)

77-4027 **Macrophage Plasminogen Activator: Induction by Concanavalin A and Phorbol Myristate Acetate.** (Eng.) Vassalli, J. D. (Rockefeller Univ., New York, NY 10021) Hamilton, J.; Reich, E. *Cell* 11(3): 695-705; 1977.

The production of plasminogen activator by peritoneal macrophages from unprimed, endotoxin-primed, and thioglycollate-primed mice was investigated. The synthesis and secretion of plasminogen activator by cultured macrophages were induced and stimulated by concanavalin A and phorbol myristate acetate and inhibited by glucocorticoids, mitotic inhibitors, and compounds affecting cyclic AMP metabolism. By manipulation of the stimulatory and inhibitory influences, enzyme production could be modulated continuously over a 200-fold range. In the same way, the proportion of cells that secreted detectable levels of enzyme could be varied from 1% to 90%. No comparable modulation of lysozyme or acid hydrolase production was observed under the same conditions. These results suggest that the physiological control of macrophage plasminogen activator production is achieved by the interacting effects of mutually antagonistic stimuli. This emphasizes the utility of this enzyme for the study of regulatory phenomena, including those relating to inflammation. (28 refs.)

77-4028 **The Presence of Two Fc Receptors on Mouse Macrophages: Evidence from a Variant Cell Line and Differential Trypsin Sensitivity.** (Eng.) Unkeless, J. C. (Rockefeller Univ., New York, NY 10021) *J Exp Med* 145(4): 931-947; 1977.

By a complement-dependent selection protocol, a stable variant of a clone of the $P388D_1$ macrophage line was isolated using four cycles of treatment with mouse IgG2a (15 μg/ml)-rabbit anti-κ (10 μg/ml) complexes and rabbit complement (20%). At these concentrations, there was max cytotoxicity (98%-99%) of the initial cells (5-10 x 10^6). The number of high-affinity binding sites in the variant was 10% that of the parent, and the Ka of the rabbit IgG complexes for the variant was always three times higher than that of the parent. Although the number of sites per cell and the Ka of the high-affinity site for rabbit IgG in antigen-antibody complexes were altered in the variant, the binding of monomeric IgG2a was unchanged in both respects. These results provide evidence for the presence of two distinct Fc receptors. The two receptors could also be distinguished on the $P388D_1$ line and on thioglycollate-induced mouse peritoneal macrophages by differential sensitivity to trypsinization. The receptor that binds monomeric IgG2a, sheep RBC (SRBC) covalently bound with IgG2a or rabbit IgG using glutaraldehyde, and Sephadex beads coupled with IgG2a or rabbit IgG using cyanogen bromide activation is sensitive to trypsinization. The receptor that binds soluble rabbit antibody-antigen complexes, trinitrophenyl-SRBC, and dinitrophenyl DNP-bovine serum albumin Sephadex beads coated with rabbit anti-DNP IgG is trypsin-resistant. Thus, unlike rabbit IgG in antigen-antibody complexes, uncomplexed rabbit IgG binds to a trypsin-sensitive Fc receptor. This suggests that conformational changes induced by the binding of ligand may be important to macrophage function. (41 refs.)

77-4029 **Aggregation of Intramembranous Particles During Formation of Fc and C3 Rosettes (Meeting Abstract).** (Eng.) Douglas, S. D. (Univ. Minnesota Medical Sch., Minneapolis, MN 55455) Ooka, M. P. *Fed Proc* 36(3): 1314; 1977. (no refs.)

77-4030 **Subclass Specificity for the Binding of Murine Myeloma Proteins to Cells Bearing Fc Receptors (Meeting Abstract).** (Eng.) Titus, J. A. (NIH, Bethesda, MD 20014) Segal, D. M. *Fed Proc* 36(3): 1314; 1977. (no refs.)

77-4031 **The Distance Between the Contact Sites for DNP and Menadione Ligands in the Combining Region of Myeloma Proteins Binding Both Haptens. I. Estimation of Distance by Fluorescent Energy Transfer in Protein 460.** (Eng.) Manjula, B. N. (Dept. Internal Medicine, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT 06510) Richards, F. F.; Rosenstein, R. W. *Immunochemistry* 13(11): 929-937; 1976.

The distance between the contact sites forξ-2,4-dinitrophenyllysine (Dnp) and Menadione thioglycolate (Men) in the combining region of protein 460 (a mouse γA_2 myeloma immunoglobulin) was measured. It had been previously shown that protein 460 contains a heavy-chain cysteine residue close to the antibody combining region. This chain was substituted with two fluorescent donor probes, and the energy transfer between the donor probe and each of the two haptens bound to protein 460 was measured using nanosecond fluorimetry. From the energy transfer data, it was calculated that the minimum distance between the Dnp and Men binding sites is not $<$ 11.4 A. It is concluded that the binding region of protein 460 has distinct subsites at which the two haptens are bound. (36 refs.)

77-4032 **Distance Between the Contact Sites for DNP and Menadione Ligands in the Combining Region of Myeloma Proteins Binding Both Haptens. II. Estimation of Distance Using Haptenic Probes with Variable Length Spacers.** (Eng.) Rosenstein, R. W. (Dept. Internal Medicine, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT 06510) Richards, F. F. *Immunochemistry* 13(11): 939-943; 1976.

The binding of proteins 315 and 460 (IgA_2 mouse myeloma immunoglobulins) to a series of 2,4-dinitrophenyl (Dnp)- and Menadione-based solid-phase immunoabsorbents with different length spacer groups (to which the Dnp and Menadione groups were attached) was studied to determine how deep in the combining region each hapten binds. Proteins 315 and 460 share similar combining region dimensions with respect to the haptens used. Menadione bound in the combining regions of both proteins at a depth of 22 A; Dnp bound at a depth of 8.8 A in protein 460 and 11 A in protein 315. The difference between these values, 11-13 A, measures the separations between the contact sites for these two haptens. They agree with values obtained independently from energy transfer data. The results suggest that the antigen binding sites of the two myeloma immunoglobulins are composed of distinct subsites or contact regions, each capable of binding a different hapten group. Multifunctional binding of antigens may not be restricted to myeloma proteins, and it probably has biological importance. (25 refs.)

77-4033 **Amino Acid Sequence of the First Hypervariable Region of 2κ and Aλ Bence Jones Cryoglobulin.** (Eng.) Meinke, G. C. (Dept. Immunopathology, Scripps Clinic and Res. Foundation, La Jolla, CA 92037) Spiegelberg, H. L. *Immunochemistry* 13(11): 915-919; 1976.

Three monoclonal Bence Jones protein cryoimmunoglobulins (immunoglobulins that precipitate in the cold), namely, two κ proteins of the VKI subgroup and one λ protein of the V λIII subgroup, were sequenced to 40 residues from the NH_2-terminal end to determine if they share common sequences in the variable regions that could be responsible for their precipitation in the cold. One of the κ proteins and the λ protein had several rare substitutions in relatively constant positions in the variable region, but the sequence of the second κ protein was unremarkable. In the first hypervariable region, the two κ proteins had Asx at position 31; all three proteins had Tyr at position 32. However, a noncryoprecipitating VKI Bence Jones protein was also found to have Asp and Tyr in positions 31 and 32. It is concluded that the structural requirements for cryoprecipitation of light chains are probably complex and not the result of similar amino acid sequences in the variable regions. (49 refs.)

77-4034 **Amino Acid Sequence of the NH_2-Terminal Extra Piece Segments of the Precursors of Mouse Immunoglobulin λ-Type and κ-Type Light Chains.** (Eng.) Burstein, Y. (Dept. Organic Chemistry, Weizmann Inst. Science, Rehovot, Israel) Schechter, I. *Proc Natl Acad Sci USA* 74(2): 716-720; 1977.

The messenger RNA molecules coding for mouse immunoglobulin light (L) chains direct the cell-free synthesis of precursors in which extra peptide segments precede the amino termini of the mature proteins. The results of amino acid sequence analyses of two precursors labeled with 20 radioactive amino acids enabled the unambiguous determination of the complete primary structure of the extra-piece segments. The complete sequence (and size) of the NH_2-terminal extra piece in the MOPC-104E λ L-chain precursor is Met-Ala-Trp-Ile-Ser-Leu-Ile-Leu-Ser-Leu-Leu-Ala-Leu-Ser- Ser-Gly-Ala-Ile-Ser (19 residues). In the MOPC-41 κ L-chain precursor, the sequence is Met-Asp-Met-Arg-Ala-Pro-Ala-Gln-Ile-Phe-Gly-Phe-Leu-Leu-Leu- Leu-Phe-Pro-Gly-Thr-Arg-Cys (22 residues). The extra pieces in the precursors of MOPC-104E (λ), MOPC-41 (κ), and MOPC-321 (κ) L chains differ extensively from each other in their amino acid sequence (65%-73%). In addition to this sequence heterogeneity, the extra pieces are characterized by a high percentage of hydrophobic residue. The marked hydrophobicity of the extra piece suggests that it may favor interaction of the precursor with cell membranes, in a manner similar to the function of the "hydrophobic domain" of membrane-bound proteins. Two possible targets for the interaction are the endoplasmic membranes, where the NH_2-terminal extra piece is cleaved from the precursor to yield mature protein destined for secretion, and the cell surface membrane, where the intact precursor is anchored by the hydrophobic extra piece to serve as the antigen-recognizing receptor. (28 refs.)

77-4035 **Absence of Lysine from the DNP-Lysine Binding Site of Protein 315; Designation of Lysine 52 of the Heavy Chain as a Peripheral Residue.** (Eng.) Klostergaard, J. (Dept. Immunology Res., Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263) Grossberg, A. L.; Krausz, L. M.; Pressman, D. *Immunochemistry* 14(1): 37-44; 1977.

The relation of lysine 52 of the heavy chain of protein 315 to the dinitrophenyllysine combining site of the protein was studied. Protein 315 was obtained from the serum of female BALB/c mice with myeloma tumor MOPC-315. Results indicate that neither lysine 52 nor any other lysine is involved in the contact region of the combining site. Samples of protein 315 were acylated with maleic anhydride in the presence and absence of the protecting hapten ε,N-dinitrophenylaminocaproic acid. The binding was studied by equilibrium dialysis against ε N-dinitrophenyl-L-lysine. Different concentrations of protein, maleic anhydride, and hapten were studied to determine their effects on the number of binding sites remaining, and on the magnitude of the binding constants. The maleylated preparations show only a small loss of sites, whether hapten-protected or not. The results indicate that if lysine 52, which is involved in covalent bond formation with α, N-bromoacetyl- ε, N-dinitrophenyl-L-lysine (BADL), were part of the site, then protein 315, in which lysine 52 was maleylated in the presence of the hapten, should incorporate BADL as an affinity label, and protein 315, in which lysine 52 was maleylated in the absence of hapten, should not. However, both do, to the same extent. (24 refs.)

77-4036 **Thymosin α : Isolation and Sequence Analysis of an Immunologically Active Thymic Polypeptide.** (Eng.) Goldstein, A. L. (Div. Biochemistry, Univ. Texas Medical Branch, Galveston, TX 77550) Low, T. L.; McAdoo, M.; McClure, J.; Thurman, G. B.; Rossio, J.; Lai, C. Y.;

Chang, D.; Wang, S. S.; Harvey, C.; Ramel, A. H.; Meienhofer, J. *Proc Natl Acad Sci USA* 74(2): 725-729; 1977.

The amino acid sequence of a biologically active polypeptide isolated from calf thymus, termed thymosin α , was determined. Thymosin α is a heat-stable, highly acidic molecule composed of 28 amino acid residues. This peptide is one of several present in thymosin fraction 5 that may participate in the regulation, differentiation, and function of lymphocytes. A nomenclature is suggested for the family of polypeptides present in thymosin fraction 5. (35 refs.)

See also:

* (Rev.): 77-3601, 77-3647, 77-3651, 77-3662, 77-3663, 77-3664, 77-3692.

* (Chem.): 77-3758, 77-3759, 77-3813.

* (Phys.): 77-3839, 77-3840, 77-3841, 77-3843.

* (Viral): 77-3875, 77-3879, 77-3893, 77-3908, 77-3922, 77-3925, 77-3931, 77-3944, 77-3945, 77-3946, 77-3947, 77-3952.

* (Path.): 77-4044, 77-4063, 77-4064, 77-4066, 77-4110, 77-4111, 77-4112, 77-4113, 77-4114, 77-4117, 77-4118.

PATHOGENESIS

77-4037 **Alkalotic Disequilibrium in Patients with Solid Tumors: Rediscovery of an Old Finding.** (Eng.) Harguindey, S. (Roswell Park Memorial Inst., Dept. Medicine A, 666 Elm St., Buffalo, NY 14263) Speir, W. A.; Kolbeck, R. C.; Bransome, E. D. *Eur J Cancer* 13(8): 793-800; 1977.

The acid-base equilibrium in two groups of cancer patients, 32 with newly diagnosed bronchogenic cancer and 11 with various solid tumors, was compared with that in 18 normal volunteers and 83 hospitalized patients with diverse diseases. A consistent tendency toward alkalosis was found in both groups of cancer patients. Similar findings reported in the literature of 40-70 yr ago are discussed, and the possible biochemical implications of these findings are considered. These findings obtained with modern technology should encourage studies of the effects of alkalinity in the pathogenesis and progression of cancer. (32 refs.)

77-4038 **Cushing's Syndrome Associated with Bronchial Adenoma.** (Eng.) Eastridge, C. E. (1030 Jefferson Ave., Memphis, TN 38104) Fields, M. L.; Young, J. M. *Am J Surg* 133(2): 236-239; 1977.

A case of Cushing's syndrome due to adrenocortical hyperplasia resulted from a slowly growing peripheral bronchial adenoma that was recognized as the source of ACTH and melanocyte-stimulating hormone (MSH) secretion 8 yr after bilateral adrenalectomy. A 56-yr-old man was seen for evaluation of a peripheral nodular lesion in the right lower lung, 8 yr after bilateral adrenalectomy for Cushing's disease. Urinary 17-ketosteroids and 17-hydroxycorticosteroids were elevated. The nodule was excised, and microscopic sections revealed an adenoma consisting of small cells with hyperchromatic nuclei, scanty cytoplasm, and infrequent mitoses. Assay revealed an ACTH content of 307 milliunits/g wet tissue and an MSH content of 7.2 units/g. It is concluded that the tumor was able to synthesize and release substances that are chemically and biologically similar to ACTH and MSH. Stimulation of the adrenal cortex by this material resulted in hyperplasia and hypersecretion, and stimulation of the melanocytes by MSH resulted in excessive pigmentation. (14 refs.)

77-4039 **Ultrastructure in the Differential Diagnosis of Pulmonary Histiocytosis and Pneumocystosis.** (Eng.) Gold, J. (Dept. Lab. Medicine and Pathology, Box 76, Mayo Memorial Building, Univ. Minnesota, Minneapolis, MN 55455) L'Heureux, P.; Dehner, L. P. *Arch Pathol Lab Med* 101(5): 243-247; 1977.

The case of an infant boy is presented to demonstrate some of the clinical, radiographic, and histologic difficulties encountered when the lungs are affected by both histiocytosis X and pneumocystosis. Histiocytosis was first diagnosed at 4 mo of age when a skin biopsy was taken of a maculopapular rash. An open biopsy of the liver was performed because of hepatomegaly, and the specimen showed involvement by histiocytosis X. Treatment with prednisone and vincristine sulfate was instituted, and the cutaneous involvement cleared. At 7 mo of age the child developed cyanosis and severe respiratory distress. Antibiotic therapy was ineffective, and an open lung biopsy was performed. Pulmonary histiocytosis was diagnosed, and therapy with methotrexate and cyclophosphamide was initiated. Recurrent episodes of respiratory insufficiency necessitated hospitalization between the ages of 7 and 16 mo. At 14 mo osteolytic lesions in the skull were noted, and at 16 mo splenomegaly was found. The respiratory status continued to deteriorate and a second lung biopsy showed *Pneumocystis carinii.* Treatment with prednisone, cyclophosphamide, methotrexate, and vinblastine sulfate was reduced, and a 2-wk course of pentamidine isethionate was given. The child was discharged and he did reasonably well for several weeks, but then he became febrile, tachypneic, and cyanotic. A third lung biopsy of the left lingula showed histiocytosis X. Cyclophosphamide (50 mg) and methotrexate (5 mg) were administered. The symptoms were relieved initially, but they eventually worsened and the patient died at the age of 22 mo. At autopsy there was no evidence of *P. carinii,* but histiocytosis X was found in the thymus, skull, spleen, and bone marrow. (18 refs.)

77-4040 **Tonofilaments in Normal Human Bronchial Epithelium and in Squamous Cell Carcinoma.** (Eng.) Inoue, S. (Dept. Pathology, McGill Univ., 3775 Univ. St., Montreal, Quebec, Canada H3A 2B4) Dionne, G. P. *Am J Pathol* 88(2): 345-354; 1977.

The tonofilaments observed in the cells of squamous cell carcinoma of human bronchial epithelium were compared with those in normal bronchial epithelium in two patients. Only small numbers of tonofilaments were observed in normal tissue, and these were found only in the basal cells of the epithelium. In the tumor cells, the quantity of filaments increased considerably. They appeared in the cytoplasm as branching and anastomosing bundles (tonofibrils) and also as single filaments about 40 A thick. These bundles were particularly well-developed in the core of narrow cytoplasmic processes of tumor cells. The thickness and appearance of the single tonofilaments were similar to those of the cytoplasmic microfilaments also observed. The development of tonofilament bundles in the cytoplasmic processes of tumor cells may provide a direct motive force for deformation of the shape of the cell and the potential invasiveness of these tumor cells. (20 refs.)

77-4041 **Ultrastructure of Localized Fibrous Mesothelioma of the Pleura: Report of a Case with Histogenetic Considerations.** (Eng.) Osamura, R. Y. (Dept. Pathology, Tokai Univ. Sch. Medicine, Boseidai, Isehara-City, Kanagawa, Japan) *Cancer* 39(1): 139-142; 1977.

An electron microscope study of a localized pleural fibrous mesothelioma from a 22-yr-old woman revealed the presence of epithelial cells and fibroblasts. The findings support the concept of a mesothelial origin for this tumor. (10 refs.)

77-4042 **Malignant Neoplasms Metastatic to Gingivae.** (Eng.) Ellis, G. L. (Veterans Admin. Hosp., 5901 E. 7th St., Long Beach, CA 90822) Jensen, J. L.; Reingold, I. M.; Barr, R. J. *Oral Surg* 44(2): 238-245; 1977.

The case histories of two men aged 58 and 27 yr who developed gingival metastases of an adenocarcinoma of the lung and a synovial sarcoma, respectively, are presented. This type of metastasis is rapidly fatal. (24 refs.)

77-4043 **The Oral Melanotic Macule.** (Eng.) Page, L. R. (Dept. Periodontics, Univ. Kentucky Medical Center, Coll. Dentistry, Lexington, KY 40506) Corio, R. L.; Crawford, B. E.; Giansanti, J. S.; Weathers, D. R. *Oral Surg* 44(2): 219-226; 1977.

A review of 80 oral melanotic lesions indicates that they occur over a wide age range but primarily in adults. Most of the lesions are solitary and located in the gingiva; almost all occur in Caucasians, and there is no sex bias. Limited follow-ups indicate no serious sequelae. (8 refs.)

77-4044 **The Relationship Between Expression of Epithelial B-like Blood Group Antigen, Cell Movement and Cell Proliferation.** (Eng.) Mackenzie, I. C. (Coll. Dentistry, Univ. Iowa, Iowa City, IA) Dabelsteen, E.; Zimmermann, K. *Acta Pathol Microbiol Scand [A]* 85(1): 49-56; 1977.

Healing wounds in the oral mucosa of rhesus monkeys were examined (1) by an immunofluorescence staining method to demonstrate the distribution of a blood-group antigen cross reacting with human group B and (2) by labeling with tritiated thymidine to localize areas of cell proliferation. Within hour, blood-group antigen reactivity was lost from epithelial cells adjacent to the wound margin. Reactivity was absent from the epithelial outgrowth into the wound, but returned with restoration of epithelial continuity. The zone of incrased cell proliferation lay adjacent to, but outside of, the area of antigen loss. Antigen loss appeared to be associated with an area of increased cell movement, a finding that supports the concept that altered blood-group antigen reactivity in epithelial tissues reflects a common increased potential for cell mobility in tumors and wounds. (35 refs.)

77-4045 **Nuclear Anomalies in Organ Cultures of Human Malignant Melanomas.** (Ger.) Hecker, D. (Abteilung fur Angewandte Tumorbiologie der Geschwulstklinik, Bereich Medizin--Charite der Humboldt-Universitat, DDR-104 Berlin, Schumannstrasse 20/21, E. Germany) Rose, H.; Powitz, A. *Zentralbl Chir* 102(6): 362-366; 1977.

Ultrastructural studies of human malignant melanomas cultivated in vitro showed cytoplasmic nuclear invaginations of different depths. A possible correlation between the invaginations and an increase in nuclear membrane surface is indicated. No increase in tumor cell mitochondria that would point to increased nuclear fragmentation was found. Whether the large nuclear fragments connected by membrane bands are completely separated from each other and form amitotic multinuclear cells or whether they present various detached tumor cells or cell nuclei requires further study. (24 refs.)

77-4046 **Moles and Melanomas (Letter to Editor).** (Eng.) Rippey, J. J. (Dept. Anatomic Pathology, Sch. Pathology, South African Inst. for Medical Res., Johannesburg, South Africa) Whiting, D. A. *Lancet* 2(8029): 137; 1977.

An investigation of 54 primary cutaneous malenomas indicated that melanomas of the trunk are most likely to contain nevus cells. Most other melanomas appear on exposed areas. These findings support the theory of the dual nature of melanomas, melanomas of nevocytic origin differing from those of melanocytic origin. (5 refs.)

77-4047 **Comparability of Histological Alterations During Carcinogenesis in Animals and Man, with Special Reference to Hepatocarcinogenesis in Fish.** (Eng.) Takayama, S. (Cancer Inst., Japanese Foundation Cancer Res., Kami Ikebukuro 1-37-1 Toshima-ku, Tokyo 170, Japan) Ishikawa, T. *IARC Sci Publ* (16): 271-286; 1977.

Studies on hepatocarcinogenesis in mammals and fish are reviewed, and their relation to liver tumors in man is considered. Hyperplastic nodules are regarded as the most important preneoplastic lesion in hepatocarcinogenesis. They are induced easily in experimental animals, especially rats and mice, by exposure to carcinogenic chemicals. Similar hyperplastic lesions found in humans with cirrhosis have been suggested to be precursors of liver cancer. Tumors with a histological appearance similar to that of mammalian liver tumors have been induced in fish, and they can be classified in much the same way as liver tumors in mammals. The small aquarium fish, *Oryzias latipes*, shows a high incidence of liver tumors after a short induction period (5-8 wk) when nitrosodiethylamine (45-145 ppm) is added to the water. Various histological types of tumors were found: well-differentiated liver-cell carcinomas, poorly differentiated liver-cell carcinomas, cholangiocellular carcinomas, and/or mixed types. There were no hyperplastic nodules, fibrosis, or cirrhosis of the liver. It is concluded that the *O. latipes* is a suitable model for comparative studies on hepatocarcinogenesis. (48 refs.)

77-4048 **Aetiology of Cirrhosis, Hepatic Fibrosis, and Hepatocellular Carcinoma.** (Eng.) Blenkinsopp, W. K. (Dept. Histopathology, St. Mary's Hosp., London W2, England) Haffenden, G. P. *J Clin Pathol* 30(6): 579-584; 1977.

Postmortem material from the years 1961-1976 were used to investigate the contribution of histology in diagnosing the etiology of cirrhosis (69 cases), severe generalized hepatic fibrosis (9), and hepatocellular carcinoma (19). Of the cirrhosis cases, there was an association with alcohol in 20, hepatitis B surface antigen (HBsAg) in 17, a_1-antitrypsin in 11, and primary biliary cirrhosis in 3 cases. No agent was found in 25 cases. Eight of these cases had double associations, HBsAg being present in all. In women, 10/20 cases were cryptogenic, 7 were alcoholic, and 1 was associated with HBsAg. In men, 15/49 were cryptogenic, 16 associated with HBsAg, 13 with alcohol, and 11 with a_1-antitrypsin bodies; of the hepatic fibrosis cases (all men), there was an association with HBsAg in 1 and a_1-antitrypsin in 4; no agent was found in 4. For hepatocellular carcinoma, there was an association with alcohol in 2, HBsAg in 4, and a_1-antitrypsin in 4; no agent was found in 6. There were two double associations, with HBsAg being found in both. Orcein and aldehyde fuchsin staining gave false positive and false negative results when compared with immunofluorescence and immunoperoxidase methods for HBsAg. Large amounts of copper were found in 4 cirrhotic livers and moderate amounts in 13; there was no relationship between copper staining and etiology. (37 refs.)

77-4049 **Developmental Anomalies of the Liver and Carcinoma of the Liver in Infants and Children.** (Ger.) Cain, H. (Pathologisches Institut des Katharinenhospitals, 7000 Stuttgart 1, Kriegsberstrasse 60, W. Germany) Kraus, B.*Dtsch Med Wochenschr* 102(4): 505-509; 1977.

Several forms of intrahepatic developmental anomalies were found on histological examination in 40 children, among them several siblings and polyovular twins. These anomalies affect in principle all structural elements of the liver. In several cases--some of them complicated by cholangitis--there was cholangiofibrosis and cholangiodysplastic pseudocirrhosis. In addition, six children developed hepatocellular carcinoma between the ages of 6 mo and 12 yr. During the development of this carcinoma, obligatory nodular foci occur. They are made up of light, glycogen-loaded, epithelial cells that are transformed into small, atypical, basophilic cells. These dark cells have a high mitosis rate, having escaped from the physiological regulation of proliferation. Presumably, the various embryonic disorders of the liver structure and liver carcinoma are based on the action of the same causative factor. It may be of a toxic chemical origin and transferred across the placenta. (14 refs.)

77-4050 **Morphogenesis of Pancreatoblastoma, Infantile Carcinoma of the Pancreas: Report of Two Cases.** (Eng.) Horie, A. (Div. Pathology, Kyushu Cancer Center, 595 Notame, Minamiku, Fukuoka 815, Japan) Yano, Y.; Kotoo, Y.; Miwa, A. *Cancer* 39(1): 247-254; 1977.

Two cases of infantile carcinoma of the pancreas were diagnosed morphogenetically as pancreatoblastoma. These encapsulated tumors adhered to the head of the pancreas and to the descending portion of the duodenum. Histologic examination revealed an organoid structure composed of cords or nodules of squamous cells with elongated nuclei arranged in a parallel fasciculating pattern (squamous corpuscles), surrounding tubular structures of columnar epithelial cells, and intermediate light cell masses with little differentiation. Electron microscopy revealed zymogenlike granules and a well-developed granular endoplasmic reticulum in the cytoplasm. No detectable islet cells were detected in the tumor tissue. Both tumors could have derived from the ventral pancreas, isolated by a lack of communication with the duct of Wirsung. The duct of Santorini was patent. Because of the favorable prognosis after surgery, these tumors should be differentiated from the usual adenocarcinoma of the pancreas occurring in adults. (15 refs.)

77-4051 **A Transplantable Insulinoma in the Rat.** (Eng.) Chick, W. L. (Elliot P. Joslin Res. Lab., Harvard Medical Sch., 170 Pilgrim Road, Boston, MA 02215) Warren, S.; Chute, R. N.; Like, A. A.; Lauris, V.; Kitchen, K. C. *Proc Natl Acaa Sci USA* 74(2): 628-632; 1977.

A transplantable insulinoma was developed in inbred NEDH albino rats. The original tumor, 1 cm in diameter, was removed from the pancreas of a male parabiont 566 days after 1,000 rads of total-body x-irradiation. The time required for implanted fragments to grow to 0.5-1.5 cm in diameter decreased from 5-8 mo in the first generation to 2-5 mo in the seventh generation. Transplantation was much more successful in male animals followed for 4 mo or more than in female animals followed for a similar period (96% vs 69%). Light and electron microscopy revealed that the tumors consisted predominantly of well-granulated beta cells. Ultrastructural studies also showed small numbers of D cells. Tumor extracts contained an av of 223 units of immunoreactive insulin and

25.9 μg of immunoreactive somatostatin/g/wet wt of tissue. The tumors generally produced increasingly profound hypoglycemia within 2-4 mo following transplantation, with plasma glucose levels frequently falling to 40 mg/100 ml or lower prior to death. Removal of tumors from chronically hypoglycemic animals resulted in transient rebound hyperglycemia with plasma glucose levels > 300 mg/100 ml within the first 24 hr and a gradual decline to normal levels of 129 mg/100 ml in 2-4 days. These observations correlated with findings of marked atropy and degranulation of the beta cells in the pancreata of tumor-bearing animals and with gradual return of normal light microscopic morphology following tumor removal. (30 refs.)

77-4052 **Early Lesions of Pancreatic Ductal Carcinoma in the Hamster Model.** (Eng.) Pour, P. (Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NB 68105) Althoff, J.; Takahashi, M. *Am J Pathol* 88(2): 291-308; 1977.

Syrian golden hamsters received weekly sc injections of 10 mg/kg N-nitrosobis(2-oxopropyl)amine for life (Group 1) or 6 wk (Group 2) and were sacrificed at biweekly intervals from 2 wk (Group 1) and 8 wk (Group 2) after initiation of the experiment. The pancreas was examined in step sections, and the sequential alterations noted for each interval were recorded. Lesions were found in the intrapancreatic and extrapancreatic ducts. Equivalent alterations consisting of hyperplasia, metaplasia, atypia, and lesions characteristic of carcinoma in situ developed ubiquitously and simultaneously in pancreatic ducts of different sizes and in ductules, but not in acinar cells. The most significant finding was the formation of intrainsular ductules; their proliferation and sequential malignant alteration were comparable to the involved preexisting ductules. Differences between the two experimental groups were of a quantitative rather than qualitative nature. The incidence and multiplicity of neoplastic lesions at each interval according to group, sex, and anatomic location of the adenocarcinomas are outlined. Predilected areas for some lesions were found. The results indicate a common origin of all induced tumors from a pluripotent cell populating the pancreatic ductal system. (24 refs.)

77-4053 **Alterations of Intercellular Junctions in Spontaneous Acinar Cell Carcinoma of the Canine Pancreas (Meeting Abstract).** (Eng.) Banner, B. F. (Rush Medical Coll., Chicago, IL) Alroy, J.; Pauli, B. U.; Weinstein, R. S. *Am J Pathol* 86(2): 77a; 1977. (1 ref.)

77-4054 **Histogenetic Types and Size of Polypoid Lesions in the Stomach, with Special Reference to Cancerous Change.** (Eng.) Kozuka, S. (Dept. Pathology, Nagoya Univ. Sch. Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466, Japan) Masamoto, K.; Suzuki, S.; Kubota, K.; Yokoyama, Y. *Gann* 68(3): 267-274; 1977.

A total of 473 polypoid lesions of the stomach obtained from 297 patients were examined histologically. The max diameter of each lesion was measured. Histological gradation based on the extent of epithelial pseudostratification was used to indicate the development of a polypoid lesion. The polypoid lesions were also classified histogenetically into metaplastic and gastric types. The latter type was subdivided into a pure form and a mixed form with secondary metaplasia. The metaplastic polypoid lesions revealed a clear correlation between size and histological grade and showed a high incidence of cancerous lesions. Almost all polypoid lesions of this group had a diameter < 20 mm in the grades below V. Of the gastric polypoids, the pure form not associated with intestinal metaplasia rarely underwent malignant change, and the av size of the lesions in each grade was larger than that of the metaplastic type. Approx 10% of the pure gastric lesions of Grades I, II, and III had diameters > 20 mm. The gastric type with secondary metaplasia resembled both the metaplastic and pure gastric types in terms of size as well as malignant potential. (20 refs.)

77-4055 **Relation Between Malignancy of Polypous Adenomas of the Stomach and Their Number and Localization.** (Rus.) Lukinykh, A. K. (Dept. General Surgery, I. P. Pavlov Riazan Medical Inst., Riazan, USSR) *Klin Med (Mosk)* 55(2): 35-41; 1977.

A total of 707 patients with polypous adenomas of the stomach were reviewed. Three clinical stages of the disease were recognized: 452 patients had benign adenomas (247 solitary adenomas, 179 multiple adenomas, 26 adenomatosis); 24 patients had intermediate proliferative adenomas (11 solitary adenomas, 12 multiple adenomas, 1 adenomatosis); and 231 patients had malignant disease (85 solitary adenomas, 142 multiple adenomas, 4 adenomatosis). Surgery was performed in 447 patients, 202 of which showed malignant transformation of the adenomas. This process was observed in 74/192 patients with solitary adenomas, 124/229 patients with multiple adenomas and 4/26 patients with adenomatosis. Adenomas located in the upper and middle thirds of the stomach underwent transformation more frequently than adenomas in the lower third of the stomach (113/181 and 80/255, respectively). Patients with extended lesions of the stomach wall (anterior and posterior wall, greater and lesser curvature) underwent transformation more often (36/49) than patients with adenomas located only in the anterior wall (30/91), posterior wall (45/103), smaller curvature (32/89), or greater curvature (26/63). Surgical treatment is recommended for patients with polypous adenomas in the middle and upper thirds of the stomach. (27 refs.)

77-4056 **Cell Cycle Parameters in Human Colon: Comparison Between Primary and Recurrent Adenocarcinomas, Benign Polyps and Adjacent Unaffected Mucosa.** (Eng.) Bleiberg, H. (Interdisciplinary Group for Digestive Cancer, Dept. Internal Medicine, Institut Jules Bordet, 1, Rue Heger Bordet, 1000 Brussels, Belgium) Salhadin, A.; Galand, P. *Cancer* 39(3): 1190-1194; 1977.

The duration of the S phase and the labeling index (LI) were measured in adenocarcinomas, in polyps, and in the adjacent unaffected mucosa of the same patient. The in vitro double-labeling technique was employed. The S-phase duration in tumors was significantly longer than that in unaffected mucosa and polyps. This agrees with previously reported data on human skin, colon and rectum and supports the suggestion that a long S phase might correlate with carcinogenesis. The LI in the mucosa adjacent to the tumors was higher than that of normal tissue. Following colectomy however, the LI in the unaffected mucosa and tumor was lower than that prior to surgery. This suggests the disappearance of a systemic factor (perhaps linked to the colon) that stimulates proliferative activity in the rectal and colonic mucosa. The maintenance of a lengthened S phase in the recurrent tumor where the LI is lower indicates that proliferation rate and S-phase duration are regulated by separate control factors. (29 refs.)

77-4057 **Penetrance and Expressivity of the Gene Responsible for the Gardner Syndrome.** (Eng.) Naylor, E. W. (Bell Facility, State Univ. New York at Buffalo, Post Office Box U, Station B, Buffalo, NY 14207) Gardner, E. J. *Clin Genet* 11(6): 381-393; 1977.

Gardner's syndrome (GS), multiple polyposis of the colon associated with various soft- and hard-tissue tumors, is controlled by an autosomal dominant gene. A more complete estimation of the penetrance of the GS gene is given, based on data from the original Utah kindred described in the 1950's. The family consists of 188 members spread over 6 generations, 28 of whom inherited the syndrome. Two methods were used to calculate gene penetrance, a statistical concept of the regularity with which a gene produces its effect: the first is based on a 1:1 ratio of normal to affected persons, and the second is based on the proportion of affected individuals in sibships of different sizes. These procedures gave penetrance values of 101.9% and 100.8%, respectively. The values were confirmed by analysis of 160 additional sibships from the literature. The clinical expression of the manifestations associated with GS was tabulated for the Utah kindred. There was great variation in the time of onset and extent of clinical expression for all manifestations: epidermoid cysts, osteomas, dental anomalies, fibromas, desmoid tumors, polyposis, and adenocarcinoma. The variations suggest that independent factors such as bowel infection, diet, and other genetic background might influence gene expression. Several other tables of data are included. (58 refs.)

77-4058 **Benign (Nonpolypoid) Mucosal Changes Adjacent to Carcinomas of the Colon. A Light Microscopic Study of 20 Cases.** (Eng.) Saffos, R. O. (Univ. Hosp. Jacksonville, 655 W. Eighth St., Jacksonville, FL 32209) Rhatigan, R. M. *Hum Pathol* 8(4): 441-449; 1977.

Nonpolypoid mucosal changes found adjacent to 20 randomly selected carcinomas of the colon, as detected by light microscopy, are presented. All neoplasms were primary infiltrating and ulcerated adenocarcinomas, and all were at least at Duke's Stage B. The av age of the patients was 66 yr; 4 were white and 16 were black. A summary of the changes and a comparison with normal mucosa are tabulated. Consistent changes were not noted in the surface epithelium. However, in half the cases there was an increase in goblet cells and corresponding decrease in absorptive cells. In all cases there was an increase in crypt length (range 0.8-2 mm, vs 0.5-0.8 mm for normal mucosa). Many glands were branched, and distended crypts were common. Occasionally, the glands assumed a tortuous configuration. A markedly increased number of goblet cells lined the crypts, but there were no cytologic atypia. In none of the cases were the early changes of adenomatous polyps found. Mitotic activity was confined to the lower half of the elongated crypts. Consistent changes were not noted in the lamina propria. These changes were present consistently, refuting earlier implications that the nonpolypoid mucosa immediately adjacent to carcinomas are normal. (11 refs.)

77-4059 **Fecal Bile Acids and Cholesterol Metabolites of Patients with Ulcerative Colitis, a High-Risk Group for Development of Colon Cancer.** (Eng.) Reddy, B. S. (Naylor Dana Inst. Disease Prevention, Valhalla, NY 10595) Martin, C. W.; Wynder, E. L. *Cancer Res* 37(6): 1697-1701; 1977.

Since intraluminal constituents of the large bowel arising from dietary fats may be associated with colonic cancer development, cholesterol, cholesterol metabolites, and bile acids were estimated in feces from four subject groups. Group A was comprised of 15 patients with ulcerative colitis at high risk of colonic cancer; Group B, 15 immediate relatives of the Group A patients; Group C, 15 patients with other digestive diseases (such as Crohn's disease or spastic colon); and Group D, 40 healthy controls. Fecal bile acid levels were not significantly elevated in any group, but fecal cholesterol, coprostanol, and cholestane-$3\beta,5\alpha,6\beta$-triol levels were higher in Group A patients than in the other groups. Mean fecal cholesterol levels were 12.5, 3.3, 2.9, and 3.2 mg/g in Group A, B, C, and D, respectively, mean coprostanol levels were 26.6, 11.9, 13.8, and 12.9 mg/g, and mean cholestane-$3\beta,5\alpha,6\beta$-triol levels were 0.3, 0.05, 0.04, and 0.06 mg/g. Possible interactions between cholesterol metabolites and colonic epithelial cells may be relevant to the development of colonic cancer. (24 refs.)

77-4060 **Heritable Proximal Large Bowel Cancer (Meeting Abstract).** (Eng.) Lynch, H. T. (Creighton Univ., Omaha, NB 68178) Lynch, P. M.; Harris, R. E.; Guirgis, H. A. *Proc Am Assoc Cancer Res* 18: 270; 1977. (no refs.)

77-4061 **Mesenchymal Renal Tumors in Infants and Children: Electron Microscopic Study of Three Cases (Meeting Abstract).** (Eng.) Donnelly, W. H. (Univ. Florida Coll. Medicine, Gainesville, FL) Talbert, J. L.; Rogers, B.; Miale, T.; Hvisdala, E. *Am J Pathol* 86(2): 2a; 1977. (3 refs.)

77-4062 **The Relationship Between Nephroblastoma and Neurofibromatosis (Von Recklinghausen's Disease).** (Eng.) Stay, E. J. (Dept. Pathology, Peter Bent Brigham Hosp., Boston, MA 02115) Vawter, G. *Cancer* 39(6): 2550-2555; 1977.

Three cases of coexistent Wilms' tumor and Von Recklinghausen's disease (VRD) were documented in a series of 342 patients with nephroblastoma. In 2/3 patients, malignant transformation of the neural tumors of VRD occurred > 15 yr after radiotherapy for the Wilms' tumor. Close parallels in the associative lesions of Wilms' tumor and VRD suggest that the two entities have a common genetic basis. An embryologic association is described whereby early mutational events, ie, neural induction of nephrogenesis, may link the entities in utero. The Wilms' tumor patients in this series had a 29-fold higher incidence of VRD than that predicted for the general population. (26 refs.)

77-4063 **Metastatic Choriocarcinoma Transplanted with Cadaver Kidney: A Case Report.** (Eng.) Gokel, J. M. (Dept. Pathology, Univ. Munich, Thalkirchner Strasse 36, 8000 Munich 2, W. Germany) Rjosk, H. K.; Meister, P.; Stelter, W. J.; Witte, J. *Cancer* 39(3): 1317-1321; 1977.

A metastasizing choriocarcinoma was inadvertently transplanted to a 47-yr-old man from a female cadaver kidney. When the kidney was removed 6 days after transplantation, arterial blood vessel infiltration by choriocarcinoma cells and high levels of human chorionic gonadotropin (HCG) in the serum of the recipient indicated a hematogenous dissemination of viable neoplastic cells. Immunosuppressive therapy was discontinued after removal of the graft, and the HCG levels in the recipient gradually decreased over an 8-wk period, indicating a slow immunologic rejection of the tumor cells. The recipient committed suicide 7 mo after the transplantation had failed. No metastases were found at autopsy. It is advisable, whenever there is evidence that neoplastic cells have been transferred by a homograft, to remove the graft and discontinue immunosuppressive therapy. Neoplastic cells already disseminated can still be eliminated when the immunologic system is intact and not suppressed. (13 refs.)

77-4064 **Immunofluorescent Characterization of Rat Kidney Tumors According to the Distribution of Actin as Revealed by Specific Antiactin Antibody.** (Eng.) Hard, G. C. (Dept. Pathology, Univ. Melbourne Medical Centre, Grattan St., Parkville, Victoria 3052, Australia) Toh, B. H. *Cancer Res* 37(6): 1618-1623; 1977.

The distribution of actin in epithelial and mesenchymal tumor cells was studied in 15 mesenchymal and 10 cortical epithelial tumors induced in Porton albino Wistar rat kidneys by a single dose of dimethylnitrosamine. The histological staining pattern was examined following treatment of the tissues with human antiactin antibody and fluorescein-labeled goat antihuman α-globulin. Epithelial tumor cells demonstrated staining restricted to the peripheral sites, corresponding to the brush border region. All the various neoplastic cell forms comprising the mesenchymal tumors were characterized by cytoplasmic staining patterns that varied with cell type. Epithelial profiles in the form of tubules and islands of epithelium showed staining patterns consistent with their identity as sequestered segments of preexisting nephrons. It is suggested that the difference in actin distribution within the cell cytoplasm of mesenchymal and epithelial renal tumors might reflect their difference in local invasive growth. (19 refs.)

77-4065 **Histologic Analyses of Experimental Tumors from Mouse Blastocyst-derived Cell Lines.** (Eng.) Sherman, M. I. (Roche Inst. Molecular Biology, Nutley, NJ 07110) Miller, R. A.; Richter, C. B. *J Natl Cancer Inst* 58(4): 993-1002; 1977.

Of four cell lines derived from cultured SWR/J x SJL/J mouse blastocysts, three produced tumors in syngeneic mice at low yields. Tumors from cell line MB2 contained two kinds of cells. Most were similar to those in so-called parietal yolk sac carcinomas, they secreted Reichert's membranelike material, and they could be found in subsequent transplant generations. The other kind morphologically resembled trophoblast giant cells and did not survive transplantation. These results showed that MB2 contained cells that were either parietal endoderm cells or a closely related precursor. The tumor from line MB4 consisted of small, closely packed cells intermixed with larger cells with a foamy cytoplasm and occasional giant cells. Cells in subsequent passages of the tumor were often organized into acinar clusters. Biochemical evidence suggested that MB4 cells resembled one or both components of visceral yolk sac. Visceral yolk sac sarcomas have not been reported previously, and the MB4-derived tumor may be first. Tumors from line MB31 contained fibroblastic and epithelioid cells that could not be identified more definitely. Cultures of each tumor type contained cells morphologically characteristic of those in the originally inoculated population. The tumors produced from blastocyst-derived cell lines did not resemble the teratocarcinomas that formed when blastocysts were implanted into an ectopic site in vivo. They did not contain a wide variety of cell types, nor did they possess pluripotent embryonal carcinoma stem cells characteristic of the teratocarcinoma. That each blastocyst-derived line gave rise to a different kind of tumor suggested that each line was made up of cells trapped at some stage characteristic of the development of a particular embryonic or extraembryonic tissue. However, the presence of at least two distinct cell types in each tumor suggested that cells in the blastocyst-derived lines, although restricted in their developmental potential, may not have been determined completely. (7 refs.)

77-4066 **Experimental Yolk Sac Carcinoma (Meeting Abstract).** (Eng.) Damjanov, I. (Univ. Connecticut Sch. Medicine, Farmington, CT) *Am J Pathol* 86(2): 15a-16a; 1977. (no refs.)

77-4067 **Experimental Yolk-Sac Tumors Produced by Fetectomy Without Virus Infection in Rats.** (Eng.) Sakashita, S. (Dept. Urology, Hokkaido Univ. Sch. Medicine, Sapporo, Japan) Tsukada, Y.; Nakamura, K.; Tsuji, I.; Hirai, H. *Int J Chem* 20(1): 83-86; 1977.

A study was made to determine whether yolk-sac tumors producing α-fetoprotein (AFP) can develop in fetal membranes of rats after fetectomy alone. Pregnant WKA rats were laparotomized on the 12th day of gestation, and all fetuses were removed from the uteri, leaving the fetal membranes attached to placentas in situ, protruding into the peritoneal cavity. After 5 to 6 mo, extrauterine tumors developed in 24/30 AFP-operated rats, and elevated serum levels were detected in 19 of the tumor-bearing rats. The tumors in AFP-positive rats always contained yolk-sac tumor elements. Numerous free-floating embryoid bodies were observed in transplantable tumor lines established in the ascites form. The experiments demonstrate that yolk-sac tumors (endodermal sinus tumors) can be induced by simple fetectomy without infection by exogenous tumor virus. (13 refs.)

77-4068 **Ultrastructural Localization of Membrane Phosphatases in Teratocarcinoma and Early Embryos.** (Eng.) Damjanov, I. (Dept. Pathology, Univ. Connecticut Health Center, Farmington, CT 06032) Cutler, L. S.; Solter, D. *Am J Pathol* 87(2): 297-310; 1977.

An electron microscopic cytochemical study was performed to analyze the location of some membrane-related phosphatases in teratocarcinoma and compare it with the distribution of the same enzymes in the embryos from which these tumors were derived. Specifically, the localization of alkaline phosphatase, 5′-nucleotidase, and Mg^{2+}-activated adenosine triphosphatase (ATPase) was studied in embryo-derived teratocarcinomas and mouse egg cylinders. Alkaline phosphatase was detected in both embryonic and tumor cells, but its activity was much more intense in the tumor cells. ATPase was not seen in the embryonic ectodermal cells of 6-day-old embryos, and it was found only in occasional cells of 7- and 8-day-old embryos. No 5′-nucleotidase activity was noted in 6- to 8-day egg cylinders. There was marked ATPase and 5′-nucleotidase activity in the membranes of embryonal carcinoma cells. These data suggest some differences in the plasma membranes of embryonal carcinoma cells and equivalent embryonic cells. These differences may be significant with regard to transformation of embryonic cells into tumor cells. (23 refs.)

77-4069 **Hormone Response of Benign Hyperplastic Prostate Tissue in Organ Culture.** (Eng.) Dilley, W. G. (Dept. Surgery, Duke Univ. Medical Center, Durham, NC 27710) Birkhoff, J. D. *Invest Urol* 15(1): 83-86; 1977.

To determine whether hormonal factors may initiate and regulate the growth of prostate tumors, surgically resected tissue from 10 patients with glandular benign prostatic hyperplasia were cultured for 4 days in media containing either insulin (I), I + estradiol (E), I + testosterone (T), I + human placental lactogen (HPL), I + HPL + T, or I + human growth hormone (hGH) + T. Growth was defined by pulsing ^{3}H-thymidine on days 3-4 and determining the acid-insoluble radioactivity by scintillation counting. The I response was taken as the base value, and each patient's response to the other hormones was expressed as a percentage change from his tissue response to I. The results, divided at the 80% stimulation of growth level, showed that 7/9 specimens were stimulated by I-HPL-T, 3/6 with I-HPL, 3/7 with I-hGH-T, 4/10 with I-E, and 1/7 with I-T. The av explant cultured with I-T or I-HPL was stimulated by 31% and 48% respectively, but those cultured with I-HPL-T were stimulated by 131%. Explants cultured with I-E or I-hGH-T had intermediate levels of stimulation. The results with HPL suggest that prolactin is one of the principal hormones regulating growth of the hyperplastic human prostate. In addition, the growth stimulation seen in some specimens due to E may be related to prostate cancer. (32 refs.)

77-4070 **Multiple Threat: Second Primary Malignancies in Patients with Ovarian Carcinoma Treated with Radiation and Chemotherapy.** (Eng.) Masterson, B. J. (Kansas City, KS) Snyder, T. E. *J Kans Med Soc* 78(6): 283-285; 1977.

The hypothesis that the increased use of chemotherapeutic drugs and radiation therapy in patients with cancer may induce a second primary neoplasm was tested in a series of ovarian cancer patients treated at the University of Kansas Medical Center. Of 182 patients, 12 had multiple primaries, 11 with two and 1 patient with three. Most of the ovarian tumors in the 12 patients were diagnosed at the same time or after the discovery of the other primaries. The pattern of involvement was similar to that reported in the literature, with colon, breast, and endometrial cancer representing the second primary malignancy. This group of patients may be suspect, since the ovary is a prime site of metastatic cancer from the breast and gastrointestinal tract. Of four patients who had another primary diagnosed at the same time as the ovarian carcinoma, three had second tumors in the same organ system. Only two patients had primaries diagnosed after the discovery of ovarian cancer. One, whose case report is given, developed leukemia after an interval of 4 yr, following daily radiation therapy (5,000 rads) followed by chlorambucil (6 mg po over a 2-wk period). This medication had been discontinued 2 yr prior to discovery of the leukemia. The data show that multiple primary neoplasms are not uncommon. However, the incidence of hematologic malignancy does not ppear to be increased as a result of radiation or chemoıerapeutic drugs in this short-term follow-up survey. (11 efs.)

7-4071 **Carcinosarcoma of the Uterus.** (Ger.) Brandt, M. (Frauenklinik, Medizinische Akademie, Valkmuehlstrasse 7, DDR-50 Erfurt, E. Germany) Marzoto, F. *Zentralbl Allg Pathol* 121(1/2): 129-133; 1977.

arcinosarcomas of the uterus are rare tumors. Histological tudy of four of these tumors revealed in all a mixture of denocarcinoma cells with polymorphous mesenchymal tructures typical of carcinosarcoma. However, in one tumor, ther areas also contained sarcomatous and adenocarcinomaous components that were sharply delineated from each othr. The etiology of uterine carcinosarcomas is still uncertain. ome tumors, mullerian tumors for example, originate from he epithelium of the mullerian ducts. However, 70% of uteine carcinosarcomas probably develop by the collision of two umors that develop separately and independently. Some may riginate in locations that are not adjacent, but the more the umors progress, the more the cells intermingle. This theory s strengthened by the facts that carcinomas and sarcomas grow independently in tissue culture and that metastases conain usually only one component. (26 refs.)

77-4072 **Age-Related Changes in Iodine-Blocked Rat Breasts (Meeting Abstract).** (Eng.) Krouse, T. S. (Medical Coll. Pennsylvania, Philadelphia, PA 19129) Eskin, B. A. *Proc Am Assoc Cancer Res* 18: 79; 1977. (no refs.)

77-4073 **Multiple Primary Malignant Neoplasms and Familial Breast Cancer (Meeting Abstract).** (Eng.) Harris, R. E. (Dept. Preventive Medicine/Public Health, Creighton Univ., Omaha, NB 68178) Lynch, H. T.; Lemon, H. M.; Carney, K. *Proc Am Assoc Cancer Res* 18: 192; 1977. (no refs.)

77-4074 **The Frequency and Distribution of Mitotic Figures in Dysplasia and Carcinoma In Situ.** (Eng.) Chi, C. H. (Korean Pathology Society, Sch. Medicine Seoul Natl. Univ., Seoul, Korea) Rubio, C. A.; Lagerlof, B. *Cancer* 39(3): 1218-1223; 1977.

The frequency and topographical (ie vertical and lateral) distribution of mitotic figures in normal cervical epithelium, dysplasia, and carcinoma in situ of the uterine cervix were studied in punch biopsies and in subsequent cone specimens from 40 patients. The frequency of cells in mitosis in the whole thickness of the epithelium increased stepwise from normal epithelium to slight-moderate dysplasia, severe dysplasia, and carcinoma in situ. A difference in the frequency of mitotic figures between slight and moderate dysplasia was recorded in the superficial cell layers of the epithelium. These findings, together with earlier reported differences in the frequency of DNA-synthesizing cells between the various epithelial alterations, support the validity of the histological classification of cervical atypias. Areas with mitosis alternated with areas without mitosis, supporting previous autoradiographical findings. The possible coexistence of proliferative and nonproliferative epithelial compartments in dysplasia and in carcinoma in situ of the uterine cervix is suggested. (29 refs.)

77-4075 **Clear Cell Carcinoma of Cervix and Vagina in Progeny of Women Who Received Diethylstilbestrol: Three Cases with Scanning and Transmission Electron Microscopy.** (Eng.) Puri, S. (650 Cambridge Blvd., S.E., Grand Rapids, MI 49506) Fenoglio, C. M.; Richart, R. M.; Townsend, D. *Am J Obstet Gynecol* 128(5): 550-555; 1977.

Ultrastructural observations of three cases of clear cell adenocarcinoma of the cervix and vagina arising in the progeny of diethylstilbestrol (DES)-treated women are described. The patients were young (19, 24, and 25 yr old), and they had a history of maternal ingestion of DES during pregnancy. The tissues studied by electron microscopy were prepared from colposcopically directed biopsies. The ultrastructural features were similar in all three cases. The neoplastic cells were arranged in solid nests or glandlike structures, and the luminal plasma membranes were covered by moderate numbers of short, thick microvilli. The neoplastic cells were separated from the underlying stroma by a regular basement membrane. Neither endocervical nor squamous cells were seen, nor was there a transition between vaginal adenosis and the neoplasm. These findings are similar to those of previously reported clear cell carcinomas of the ovary and endometrium. They strongly favor an endometrial origin for the DES-associated clear cell carcinomas and a common mullerian, as opposed to mesonephric, origin for all clear cell cancers of the female genital tract. (16 refs.)

77-4076 **Primary Squamous Cell Carcinoma in an Artificial Vagina.** (Ger.) Kucera, H. (I. Universitats-Frauenklinik, Spitalgasse 23, A-1090 Vienna, Austria) Michalica, W. *Zentralbl Gynaekol* 99(5): 300-302; 1977.

Primary squamous cell carcinoma occurred in a 54-yr-old woman 33 yr after an operation for construction of an artificial vagina. During an appendectomy at age 16, it was discovered that the patient had only rudimentary inner sexual organs. At age 21, plastic surgery was performed: the vagina was dilated by splitting and the inner connective tissue was epithelialized by tampon treatment. The patient married 9 yr later and had satisfactory intercourse. Thirty-three years after the plastic surgery the patient had a vaginal discharge, first yellowish-aqueous, then bloody. Stage III infiltrating squamous cell carcinoma of the vagina was diagnosed. Radiation with Ra led to invasion of the carcinoma into the bladder, and the patient died 4 mo later. The literature shows only four other cases of primary carcinoma in an artificial vagina. (14 refs.)

77-4077 **Verrucous Carcinoma Arising from an Artificial Vagina.** (Eng.) Abrenio, J. K. (Dept. Pathology, Creighton Univ. Sch Medicine, 10th and Castelar, Omaha, NB 68108) Chung, H. I.; Pomante, R. *Obstet Gynecol* 50(1/Suppl): 18s-21s; 1977.

A unique case of verrucous carcinoma arising from an artificial vagina is reported. Vaginal reconstruction was accomplished in a 45-yr-old woman in August 1947 using a split thickness skin graft obtained from the left inner thigh. Physical examination and biopsy of white papillary growths in 1954 revealed benign squamous cell papilloma. Upon admission in July 1964 for removal of recurrent vaginal warts, condyloma acuminata was reported. Pathological examination of the artificial vagina and rectum, which were excised in September 1973, 19 yr after the first appearance of the lesions, revealed typical verrucous carcinoma. The occurrence of the lesion in the vagina, the long duration of the neoplasm without development of metastasis, and the apparent alteration of the nature of the tumor in this case are unusual characteristics of verrucous carcinoma. Whether ionizing radiation contributed to the neoplastic change remains unclear. (12 refs.)

77-4078 **Ultrastructure of the Parotid Duct. Cytochemical Studies of the Striated Duct and Papillary Cystadenoma Lymphomatosum of the Human Parotid Gland.** (Eng.) Cutler, L. S. (Dept. Oral Biology, Univ. Connecticut Health Center, Sch. Dental Medicine, Farmington, CT 06032) Chaudhry, A.; Innes, D. J. *Arch Pathol Lab Med* 101(8): 420-424; 1977.

The morphology of the striated duct of the human parotid gland and of papillary cystadenoma lymphomatosum (Warthin's tumor) was investigated by electron microscopy and electron microscopic histochemistry to help define the origin of the epithelial component of Warthin's tumor. Tissue was obtained at the time of surgery and examined ultrastructurally and cytochemically for alkaline phosphatase (AP) or ATPase activity. The tissue obtained included four Warthin's tumors and seven samples of normal parotid gland. Cytochemical investigation of the striated ducts showed that the duct was unreactive for serum AP. However, ATPase-positive cells that had the topography, shape, and cytologic features of myoepithelial cells or developing myoepithelial cells were found along the proximal portion of the striated ducts as well as the acini and intercalated ducts of the normal parotid gland. In addition, morphologically and histochemically similar cells were found in two Warthin's tumors. These observations suggest that Warthin's tumor arises from altered stem cells that are capable of differentiating into aberrant epithelial cells (oncocytes) and/or myoepithelial cells. These stem cells may reside in the intercalated ducts, the junction of the intercalated and striated ducts, or the striated ducts. (35 refs.)

77-4079 **Malignant Mixed Tumor of Salivary Origin. A Clinicopathologic Study of 146 Cases.** (Eng.) Spiro, R. H. (Head and Neck Service, Dept. Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021) Huvos, A. G.; Strong, E. W. *Cancer* 39(2): 388-396; 1977.

An attempt was made to define more precisely the criteria for diagnosis of malignant mixed tumor (MMT) of the salivary gland, using the records of 146 patients (78 females, 68 males; aged 7-86 yr) seen over a 30-yr period (1939-1968). Current concepts regarding the pathogenesis of MMT are reviewed. The site of origin was the parotid gland in 107 patients, the submaxillary gland in 23, and the minor salivary glands in 16. Seventy had previously received treatment, usually consisting of a local excision. Histologically, there were features characteristic of mixed tumors in addition to structures that give rise to metastases. The growth pattern of the latter was usually that of a solid, glandular carcinoma or an epidermoid cancer, with occasional examples of a clearly malignant spindle or mixed spindle and giant cell variant. Differentiation was predominantly along the adenocarcinomatous and squamous lines, with the former being more frequent and consistent. The earliest microscopic evidence of malignant transformation was aggregates of large, hyperchromatic, cytologically atypical cells embedded in a hyaline stromal matrix. No correlation could be made between the microscopic appearance of the tumors and their clinical behavior. Metastatic deposits (33 patients) were usually carcinomatous, and their histology mimicked that of the primary lesions. In the untreated cases, the usual presenting symptom was a painless swelling that had been present from < 1 yr (30%) to > 20 yr (20%). Although many lesions seemed to arise in preexisting benign mixed tumors, the data suggest that the de novo origin of MMT may not be as rare as surmised. (13 refs.)

77-4080 **Tumors Associated with Hypercalcemia (Meeting Abstract).** (Eng.) Garancis, J. C. (Medical Coll. Wisconsin, Milwaukee, WI) Wilson, S. D.; Limoni, A.; Evans, E. W. *Am J Pathol* 86(2): 78a; 1977. (no refs.)

77-4081 **Thyroid Carcinoma in Children.** (Eng.) Andersson, A. (Dept. Surgery, Central Hosp., S-291 85 Kristianstad, Sweden) Bergdahl, L.; Boquist, L. *Am Surg* 43(3): 159-163; 1977.

A survey was made of 24 children under the age of 15 with thyroid cancer whose cases were reported to the Swedish Cancer Registry from 1959 to 1967. There were 6 boys (av age 9 yr, 8 mo) and 18 girls (av age 12 yr, 1 mo). None had previously received roentgen treatment in the neck or in other parts of the body. However, two patients had been treated over a long period with steroids for bronchial asthma. Another patient had received long-term treatment with large doses of vitamin D for vitamin D-resistant rickets. The occurrence of thyroid nodules (struma) was the presenting symptom in 23 patients, and in the 24th the first symptom consisted of palpable lymph gland metastases in the neck. Thyrotoxicosis was absent in all patients. Tumors affected both lobes of the thyroid in 10 patients and only one lobe in 8. Sixteen children had metastases: 12 had regional lymph gland metastases only and 4 had pulmonary metastases (2 with regional lymph gland metastases); altogether, 14 had lymph gland metastases. Upon review of the histopathological data for 22 children, the following diagnoses were made: well-differentiated (13) and moderately differentiated (5) papillary carcinoma, well-differentiated (1) and moderately differentiated (2) follicular carcinoma, and medullary carcinoma (1). Treatment was with surgery plus hormone and/or irradiation therapy, and only 1/24 patients died of postoperative complications. (14 refs.)

77-4082 **Intranuclear Rodlets in an Intrathyroid Tumor Associated with Hyperparathyroidism.** (Eng.) Sherwin, R. P. (Dept. Pathology, Univ. Southern California, 2025 Zonal Ave., Los Angeles, CA 90033) Kaufman, C.; Dermer, G. R.; Monroe, S. A. *Cancer* 39(1): 178-185; 1977.

A tumor excised from the thyroid gland of a 78-yr-old woman was shown by electron microscopy to contain distinctive, intranuclear rodlets. This is the first report of these rodlets in a nonneuronal human tumor. Although the parathyroidlike hormonal activity, histopathology, and clinical course were consistent with a parathyroid adenoma, the finding of the rodlets raised the question of origin in a special, neuron-related cell of the parathyroid or thyroid. The unusual cellular granularity and the abundant interstitial fibrillae also suggested an unusual cell of origin. Alternatively, a special metabolic activity may account for the rodlets, or they may have been overlooked in prior studies of adenomas. (15 refs.)

77-4083 **Mucoepidermoid Carcinoma of the Thyroid Gland.** (Eng.) Rhatigan, R. M. (Dept. Pathology, Univ. Hosp., Jacksonville, 655 West Eighth St., Jacksonville, FL 32209) Roque, J. L.; Bucher, R. L. *Cancer* 39(1): 210-214; 1977.

A 20-yr-old euthyroid woman presented with two palpable thyroid nodules. The scintiscan showed an area of increased uptake in the isthmus corresponding with one of the palpable nodules. The uptake in the rest of the gland was diminished, including the area of the second palpable nodule, which was in the superior portion of the left lobe. Microscopic examination revealed diffuse lymphocytic thyroiditis, follicular adenoma of the isthmus, and mucoepidermoid carcinoma of the upper left lobe. No primary tumor site outside the thyroid was identified. Mucoepidermoid carcinoma of the thyroid gland has not been previously reported; the literature is reviewed briefly, and etiologic considerations are discussed. (15 refs.)

77-4084 **Thyroid Carcinoma and Concurrent Hyperthyroidism: A Study of Ten Patients.** (Eng.) Hancock, B. W. (Academic Div. Medicine, Royal Hosp., Sheffield Sl 3SR, England) Bing, R. F.; Dirmikis, S. M.; Munro, D. S.; Neal, F. E. *Cancer* 39(1): 298-302; 1977.

Ten patients (9 women and 1 man, aged 19-80 yr) with thyroid carcinoma and coexisting thyrotoxicosis were studied. In six patients, thyroid carcinoma was suspected before thyroidectomy. In 3/4 patients in whom neoplasia was not suspected before operation, the lesion was a small papillary carcinoma. Long-acting thyroid stimulator (LATS) and long-acting thyroid stimulator protector (LATSP) were detected in the serum of only 1/8 patients tested. The possible role of hyperthyroidism in initiating thyroid malignancy is discussed. (18 refs.)

77-4085 **Cytochemical Localization of Peroxidase Activity in Normal, Proliferating and Neoplastic Thyroid Tissues of Rats. An Ultrastructural Study.** (Eng.) Christov, K. (Medicinska Akademiya, Cent'r po Onkologiya, ul. Plovdiosko pole 6, Sofiya-Darvenica 56, Bulgaria) Stoichkova, N. *Acta Histochem (Jena)* 58(2): 275-289; 1977.

An ultrastructural study was made of the distribution of thyroid peroxidase (TP), an enzyme that has an important role in iodine metabolism, in the follicular cells of Wistar rats during thyroid carcinogenesis by 4-methyl-2-thiouracil (MTU: 0.1% in drinking water). In untreated rats, TP was present in the rough endoplasmic reticulum, perinuclear cisternae, microvilli, Golgi lamellae, and in small cytoplasmic vesicles. After 3 wk of treatment with MTU, however, TP activity disappeared from the cells. After 6 mo of treatment, TP activity reappeared in the same organelles as in the untreated rats. In the epithelial cells of follicular and papillary carcinomas, the enzyme was localized primarily in the rough endoplasmic reticulum, the perinuclear cisternae, and the outer membranes of microvilli. It is concluded that inhibition of TP during carcinogenesis with MTU is reversible and that the enzyme is present in neoplastic cells. (20 refs.)

77-4086 **Clinical, Histological and Electron Microscopic Findings in Neurofibromatosis (Recklinghausen's Disease) Occurring in Childhood.** (Ger.) Watzek, G. (Universitatsklinik fur Kieferchirurgie, Alser Strasse 4, A-1090 Vienna, Austria) Matras, H.; Lassmann, G.; Lassmann, H. *Wien Klin Wochenschr* 89(6): 193-198; 1977.

A follow-up study was made of the clinical symptoms and radiologic and histologic alterations in five cases of neurofibromatosis (Recklinghausen's disease) with onset in early childhood. The clinical manifestations were predominantly restricted to the face. Histologic and ultrastructural investigation revealed different types of neurofibroma: plexiform, argyrophilic, and diffuse. Correlations between clinical findings and the histologic types of neurofibromas are discussed with reference to tumor demarcation, recurrence following surgical removal, and prognosis. Definite conclusions will depend on long-term studies of a larger number of patients. (38 refs.)

77-4087 **Paragangliomas of the Head and Neck Region: A Clinical Study of 69 Patients.** (Eng.) Lack, E. E. (Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021) Cubilla, A. L.; Woodruff, J. M.; Farr, H. W. *Cancer* 39(2): 397-409; 1977.

A clinical analysis was made of 73 paragangliomas of the head and neck that occurred in 69 patients seen over a 38-yr period (1937-1975). There were 44 carotid body (CBP), 13 vagal body (VBP), and 8 jugulotympanic (JTP) paragangliomas. In addition, there were three nasal paragangliomas (NP) and one each from the larynx, orbit, and aortic arch, all of which are rare. The av age at diagnosis was 46 yr for CBP, 50 for VBP, and 58 for JTP; two patients with NP were 50 yr old, but one was 8. Neither sex predominated among the CBP patients, but women predominated in the VBP and JTP groups. With two exceptions, all patients were Caucasian. The av duration of symptoms before diagnosis was 4 yr, and the major presenting complaints were painless mass in the neck (CBP), 10th cranial nerve impairment with ipsilateral vocal cord paralysis (VBP), and progressive hearing loss and/or tinnitus (JTP). Without the aid of selective carotid angiography, needle aspiration, and incisional biopsy, a precise preoperative diagnosis of paraganglioma is difficult. Malignant behavior, as evidenced by lymph node and/or bony and visceral metastases, was observed in five patients (4 CBP and 1 VBP). In contrast to the benign tumors, the five clinically malignant paragangliomas routinely contained mitotic figures, and some showed central necrosis of the nests (Zellballen) of epithelioid cells. Less frequent findings were vascular and lymphatic invasion and nerve encasement. (38 refs.)

77-4088 **An Autopsy Case of Malignant Schwannoma of the Buttock with an Unusual Mode of Invasion Involving the CNS.** (Jpn.) Inai, K. (Dept. Pathology, Hiroshima Univ. Sch. Medicine, Hiroshima, Japan) Tokuoka, S.; Hinokida, H.; Tsuge, K. *Jpn J Cancer Clin* 23(5): 499-505; 1977.

An automobile painter who had been exposed to the atom bomb at age 1.5 yr developed a malignant schwannoma in his right buttock at age 31 yr and died 2.4 yr later. The tumor recurred twice, eventually forming a huge mass; the patient developed paralysis of the lower extremities followed by markedly increased intracranial pressure. Autopsy showed that the tumor extended into the pelvic retroperitoneal space and involved the right sciatic nerve trunk, the lumbar vertebrae, and the spinal cord. Dissemination into the arachnoid of the brain was also demonstrated by histologic examination. The patient had a small benign schwannoma on the scalp, but no definite evidence of von Recklinghausen's disease was found. (5 refs.)

77-4089 **The Biological Behavior of Experimental Tumors of the CNS.** (Ger.) Warzok, R. (Institut fur Allgemeine Pathologie und Pathologische Anatomie, Medizinische Akademie, Nordhauser Strasse 74, DDR-50 Erfurt, E. Germany) Schneider, J.; Thust, R.; Blaufuss, E. M. *Zentralbl Allg Pathol* 121(1/2): 40-54; 1977.

In 31 experimental groups 1,955 hooded and Wistar rats were given methyl-, dimethyl-, trimethyl-, and ethylnitrosourea or dimethylphenyltriazene at various doses. Altogether, 3,102 tumors resulted, 1,930 of them in the CNS. These CNS tumors comprised 574 oligodendrogliomas, 417 astrocytomas, 113 glioblastomas, 27 gliosarcomas, 167 sarcomas, and 518 neurinomas (114 not accounted for). Transplacental application of the carcinogens led to tumor formation of the CNS in 100% of the animals. In contrast to brain tumors in humans, tumor dedifferentiation in rats was of minor importance with regard to clinical course. In rats the tumors led to death within a few hours or days after appearance of the first symptoms. Isomorphous tumors occurred much more frequently after transplacental application than after application to adult animals, in which polymorphous neoplasms dominated. The histology of the tumors is described in detail, and parallels are drawn to human neuro-oncology. (34 refs.)

77-4090 **Ultrastructure of Ciliated Cells in Early Stages of Their Formation During Chemical Carcinogenesis of the CNS.** (Rus.) Mardanova, G. V. (Lab. Functional Anatomy, Inst. Human Morphology, Acad. Sciences USSR, USSR) *Arkh Anatol Gistol Embriol* 72(4): 93-97; 1977.

Pellets of 7,12-dimethylbenz(a)anthracene (DMBA) were implanted in the right hemisphere of female albino SHK rats, and brain tumor specimens were obtained 12, 24, and 48 hr later. These specimens showed profound ultrastructural changes. Precursors of ciliated cells could be observed in the perivascular tissue after 12 hr; their characteristic feature was the presence of lipidlike inclusions. At 24 hr, these cells were increased in number, and lipidlike inclusions started to form clumps in the peripheral area. A cellular edge started to form around the carcinogen pellet 48 hr after implantation: the cell layer nearest the carcinogen consisted of cells with multiple lipidlike inclusions and with elongated fingerlike cellular processes. It was suggested that these ciliated cells originate from hemopoietic stem cells. (5 refs.)

77-4091 **Ultrastructure and Cytochemical Studies on Human Tumors Secreting Catecholamines.** (Eng.) Yokoyama, M. (Dept. Urology, Branch Hosp., Faculty Medicine, Univ. Tokyo, Tokyo 112, Japan) *Acta Histochem Cytochem* 10(1): 93-111; 1977.

Correlative ultrastructural and biochemical studies on 38 human neurogenic tumors and, as control tissues, 12 adrenal medullas and 5 sympathetic ganglia revealed that the tumors had an ability to synthesize catecholamines (CA). The ultrastructure of the tumors showed that neurogenic tumors are a group of tumors of nerve cell origin at various stages of differentiations that are able to synthesize, store and secrete CA. The CA granules in the pheochromocytomas and paragangliomas were similar to those in the adrenal medulla of humans and rodents. Large-cored, small-cored, and small clear vesicles in all neurogenic tumors resembled those in the sympathetic ganglia and nerve endings. Granular resemblance suggested the similarity of CA storage in the tumors and control tissues. Double fixation with aldehyde and osmium revealed that the human adrenal medulla has cells with ellipsoidal granules (E granules) as well as cells with more or less rounded granules (R granules). Pheochromocytomas have three kinds of cells containing E granules, R granules, and granules with dense, peripherally located cores (dp granules) that resemble the noradenaline (NA) granules of rat. Chemical assay showed a predominance of E and/or dp cells in all NA-dominant tumors. Chemically mixed tumors showed a mixed type of dp/E and R cells. One adrenaline (A)-dominant tumor was R-dominant. This suggests that E and dp granules contain NA and that R granules contain A in the pheochromocytomas. The E cells in the human adrenal medulla also appear to be of the NA-storing type. (39 refs.)

77-4092 **Fine Structure of Medulloepithelioma.** (Eng.) Pollak, A. (Dept. Neuropathology, Univ. Zurich, Zurich, Switzerland) Friede, R. L. *J Neuropathol Exp Neurol* 36(4): 712-725; 1977.

The biologic characteristics of the 14 literature cases of medulloepithelioma are reviewed, and a new case is presented in which the first electron microscopic study was made. This latter case is unusual in being the second on record that originated in the cerebellum (of a 15-mo-old girl) and the first showing massive seeding along the spinal canal. The statistics emerging from the 15 cases show that the av age of onset is 4.4 yr, that there is no sex predilection (7 males, 8 females), and that there is a preference for the cerebral hemispheres (11 cases). The clinical course is rapid, leading to death within an av of 6 mo. Electron microscopic examination of the new case disclosed a very primitive, undifferentiated epithelium comprised of cuboidal or high columnar cells with relatively little cytoplasm and few organelles. Specific cell differentiation was not found. The nuclei were isonorphic, with a coarsely granular chromatin distributed uniformly throughout the nucleoplasm. The basal surface of the epithelial layer rested on a distinct, continuous, often folded basement membrane. The epithelial surface lacked cilia or microvilli, and it was covered with an irregular amorphous coat. The lateral cell surfaces lacked interdigitations, but showed extensive primitive forms of cell junctions. (28 refs.)

77-4093 **Genetic Control of Brain Tumor Growth (Meeting Abstract).** (Eng.) Albright, L. (Univ. Pittsburgh Sch. Medicine, Pittsburgh, PA) Gill, T. J. *Am J Pathol* 86(2): 22a-23a; 1977. (no refs.)

77-4094 **Retinoblastoma and Intracranial Malignancy.** (Eng.) Jakobiec, F. A. (Registry Ophthalmic Pathology, Armed Forces Inst. Pathology, Washington, DC 20306) Tso, M. O.; Zimmerman, L. E.; Danis, P. *Cancer* 39(5): 2048-2058; 1977.

Two cases of neuroblastic intracranial tumors occurring in infant patients with retinoblastoma are reported. The tumors are believed to represent second primary neoplasms. One patient with well-differentiated bilateral retinoblastomas developed, > 2 yr later, a pineal tumor composed of small neuroblastic cells and a second population of larger cells with vesicular nuclei and more abundant cytoplasm. The features of the neoplasm were unlike those of either primary or secondary retinoblastoma. In the second patient, symptoms of a brain tumor led to the discovery of a small, uniocular, well-differentiated retinoblastoma. The brain tumor was retrochiasmal, highly differentiated (showing areas of photoreceptor differentiation), and interpreted as an ectopic nonmetastatic retinoblastoma. Discussion is made of the possible histogenetic origins of the tumors. It is concluded that patients who develop brain tumor symptoms after a prolonged interval since treatment of ocular tumors should be suspected of harboring a second intracranial primary. (17 refs.)

77-4095 **Retinoblastoma: Evidence That Genetic Susceptibility to Cancer Induction May Be Related to a DNA Repair Defect (Meeting Abstract).** (Eng.) Weichselbaum, R. R. (Harvard Sch. Public Health, Boston, MA 02115) Little, J. B. *Proc Am Assoc Cancer Res* 18: 176; 1977. (no refs.)

77-4096 **A Genetic Study on Familial Retinoblastoma (Meeting Abstract).** (Jpn.) Matsunaga, E. (Natl. Inst. Genetics, Mishima, Japan) *Jpn J Hum Genet* 20(4): 281; 1976. (no refs.)

77-4097 **Methotrexate Encephalopathy: A Sequential Pathological Study (Meeting Abstract).** (Eng.) Liu, H. M. (Children's Memorial Hosp., Chicago, IL) Maurer, H. *Am J Pathol* 86(2): 57a-58a; 1977. (no refs.)

77-4098 **Occurrence of Acute Leukaemia in Myeloproliferative Disorders.** (Eng.) Rosenthal, D. S. (721 Huntington Ave., Boston, MA 02115) Moloney, W. C. *Br J Haematol* 36(3): 373-382; 1977.

Eighteen cases of well-documented acute leukemia were encountered in a series of 306 cases of myeloproliferative disorders followed over a 21-yr period. The leukemias were either acute myeloblastic or myelomonocytic, and they occurred from 6 mo to 20 yr after the initial diagnosis. The onset was relatively abrupt and the course rapidly fatal, with a median survival of 4 wk. Because of the prolonged preleukemic phase, it was possible to carry out a variety of clinical and laboratory observations. Although no consistent features were noted, dysplastic hemopoiesis, a fall in WBC alkaline phosphatase activity, the presence of the Pelger-Huet anomaly, and other abnormalities indicated a disturbance in granulocytic maturation. These findings suggest that an initial injury to a pleuripotential hemopoietic stem cell is followed by a prolonged latent period, and that acute leukemia is due to exposure to additional injurious agents or to a lack of cell-regulating factors. (13 refs.)

77-4099 **Cutaneous Vasculitis with a Myeloproliferative Disorder.** (Eng.) Kennedy, C. (Dept. Dermatology, St. George's Hosp., London SW1X 7EZ, England) Sanderson, K. V.; Wood, T. A. *Proc R Soc Med* 70(4): 284-285; 1977.

A 64-yr-old man presented with tender nodules which had been appearing for 3 mo on the dorsa of the hands and were diagnosed as cutaneous vasculitis. Blood and marrow studies showed blast cells in the peripheral circulation and the presence of an extra chromosome in the marrow. These findings confirmed the underlying myeloproliferative condition, which has been documented as leading to terminal acute leukemia. (4 refs.)

77-4100 **Pyoderma Gangrenosum with Philadelphia Chromosome-negative Chronic Myeloid Leukemia.** (Ger.) Kovary, P. M. (Universitats-Hautklinik, Von-Esmarch-Strasse 56, D-4400) Lonauer, G.; Niedorf, H.; Nautsch, C.; Pawlowitzki, I. H. *Dermatologica* 154(6): 360-366; 1977.

A 35-yr-old woman developed chronic myeloid leukemia 20 mo after the appearance of pyoderma gangrenosum (PG). Induction by cytostatic drugs used to treat the PG was excluded, confirming the association between PG and leukemia. (29 refs.)

77-4101 **Variation in the Philadelphia Chromosome.** (Eng.) Watt, J. L. (Dept. Genetics, Univ. Aberdeen, Foresterhill, Aberdeen AB9 2ZD, Scotland) Hamilton, P. J.; Page, B. M. *Hum Genet* 37(2): 141-148; 1977.

A study of 17 patients with chronic myeloid leukemia indicated that the Philadelphia chromosome is a variable entity: four unusual variants were found. The size and binding patterns of the chromosome were found to differ among individuals. (12 refs.)

77-4102 **Familial Leukaemia and SV40 Transformation (Letter to Editor).** (Eng.) McKeen, E. A. (Clinical Epidemiology Branch, NCI, Bethesda, MD 20014) Miller, R. W.; Mulvihill, J. J.; Blattner, W. A.; Levine, A. S. *Lancet* 2(8032): 310; 1977.

When a clinically normal girl in a family with six cases of acute myelogenous leukemia developed the leukemia 6 yr later, the mother said she was not surprised because the girl had developed the same odor, especially of the scalp. The odor is under investigation. The girl had increased transformation on exposure to SV40 virus in cultured skin fibroblasts while clinically normal. (1 ref.)

77-4103 **Acute Leukemia (AL) in the Course of Idiopathic Sideroblastic Anemia (IRSA) (Meeting Abstract).** (Eng.) Salem, Z. (Univ. Oakland Health Sciences Center, Oklahoma City, OK 73104) Hussein, K. K.; Bottomley, S. S. *Proc Am Assoc Cancer Res* 18: 294; 1977. (no refs.)

77-4104 **Idiopathic Acquired Sideroblastic Anemia Terminating in Acute Myelofibrosis: Case Report and Review of Literature.** (Eng.) Yeung, K. Y. (Hematology-Oncology Section, Veternas Admin. Hosp., Temple, TX 76501) Trowbridge, A. A. *Cancer* 39(1): 359-365; 1977.

The case of a 63-yr-old man with acute myelofibrosis that presented initially as idiopathic acquired sideroblastic anemia is reported. Intensive polychemotherapy with vincristine, cytosine arabinoside, and prednisome and a later trial of oxymetholone therapy were ineffective. He died 134 days after the diagnosis of acute myelofibrosis was established. The 11 previously reported cases of acute myelofibrosis are reviewed, and the relationships of acute myelofibrosis to other myeloproliferative disorders and to idiopathic acquired sideroblastic anemia are discussed. (18 refs.)

77-4105 **An Anemic Patient.** (Dut.) Dunning, A. J. (No affiliation given) *Ned Tijdschr Geneeskd* 120(28): 1212-1216; 1976.

The case of a 68-yr-old woman with acute hypoplastic myeloid leukemia is discussed. The patient was first seen for anemia resulting from a prepyloric ulcer. Hematologic studies showed 14,000 WBC/mm^3, 1.2×10^6 platelets/mm^3, and a normal differential. Two years later the woman again became anemic; there was no occult blood in the feces, the hematocrit was 22%, WBC were 800/mm^3 (98% lymphocytes), and platelets were 390,000/mm^3. After many unsuccessful attempts, a bone marrow sample was obtained. It contained many megakaryocytes and an abundance of myeloblasts, with no increase in fibroblasts. The patient was given low-dose chemotherapy. (4 refs.)

77-4106 **Osteogenic Sarcoma in a Patient with Aplastic Anemia.** (Eng.) Lascari, A. D. (Dept. Pediatrics, Southern Illinois Univ. Sch. Medicine, Post Office Box 3926, Springfield, IL 62708) Eveloff, A. R. *South Med J* 70(7): 874-875; 1977.

The case of a 14-yr-old boy who developed osteogenic sarcoma of the left thigh 13 yr after chloramphenicol-induced aplastic anemia is presented. The relationship between these diseases is discussed. (19 refs.)

77-4107 **Malignant (Fibrous) Histiocytoma Arising in Association with a Bone Infarct in Sickle-Cell Disease: Coincidence or Cause-and-Effect?** (Eng.) Mirra, J. M. (Dept. Surgical Pathology, Univ. California Center Health Sciences, Los Angeles, CA 90024) Gold, R. H.; Marafiote, R. *Cancer* 39(1): 186-194; 1977.

The case report of a 26-yr-old man with homozygous-S sickle-cell disease complicated by malignant (fibrous) histiocytoma arising within a tibial medullary infarct is presented. This is the ninth reported case of human sarcoma associated with bone infarct and the first associated with sickle-cell disease. Evidence for a causal relationship, based partly on a detailed histologic analysis of bone infarcts, is presented. (11 refs.)

77-4108 **Burkitt's Lymphoma.** (Dut.) Jansen, J. (Afdelingen Inwendige Geneeskunde, Academisch Ziekenhuis der Vrije Universiteit te Amsterdam, Amsterdam, Netherlands) van 't Veer, M. B.; van Veelen, H.; Krul, E. J.; Blok, P. *Ned Tijdschr Geneeskd* 121(4): 133-139; 1977.

The case of a 23-yr-old white man with abdominal Burkitt's ymphoma is presented. Initial treatment with cyclophosphamide produced a remission, but a recurrence began 9 wk later. Further chemotherapeutic programs with other agents caused repeated remissions followed by rapid recurrences. The patient died 9 mo after his first admission. Serum titers against Epstein-Barr virus (EBV) rose throughout the course of the disease. Histologically, the lymphoma could not be distinguished from those occurring endemically in Africa. Clinically, the age of onset and the occurrence of abdominal tumors as primary sites are higher in non-African cases. Anti-EBV titers are usually absent or lower in non-African patients. Despite these differences, the same type of tumor is probably being dealt with in both cases. (38 refs.)

77-4109 **Tumours of the Mononuclear Phagocytic System--An Ultrastructural Study of Histiocytic Lymphomas.** (Eng.) Henry, K. (Dept. Histopathology, Westminster Medical Sch., London, S.W.1., England) *IRCS Med Sci: Cancer* 5(7): 326-327; 1977.

An ultrastructural investigation of 97 non-Hodgkin's lymphomas indicated that 10/12 giant cell lymphomas were histiocytic. This is in contrast to previous reports that stated that true histiocytic lymphomas are rare. The ultrastructural features of these tumors are presented. (5 refs.)

77-4110 **Mediterranean Lymphoma. Diffuse Enteromesenteric Immunoblastic Sarcoma Without Qualitative IgA Anomaly.** (Fre.) Galian, A. (Antenne du Service Central d'Anatomie et Cytologie Pathologiques (Pr P. Roujeau), Hopital Saint-Lazare, 107, rue du Faubourg-Saint-Denis, F 75475 Paris Cedex 10, France) Scotto, J.; Rouffy, J.; James, J. M.; Lenormand, Y.; Rambaud, J. C. *Gastroenterol Clin Biol* (1): 49-58; 1977.

A 22-yr-old Algerian man was admitted for continuous abdominal pain, chronic and copious diarrhea, vomiting, and poor general condition. The digestive symptoms had started 6 yr earlier. Two years before admission, clinical and biological signs of hypoparathyroidism had been cured by vitamin D_2. Physical examination showed cachexia, leg edema, pleural and pericardic effusions, a segmented abdominal mass, and enlarged axillary nodes. Biological investigations revealed a malabsorption syndrome but no serum immunoglobulin abnormality. The patient died within a few weeks. Photon and electron microscopy study showed an immunoblastic cellular proliferation that had infiltrated the wall of the entire small intestine and destroyed the normal axillary and mesenteric lymph node architecture. Portal triads and serous effusions also contained immunoblastic cells. A few cells showed a tendency toward plasmocytic differentiation, but no intracytoplasmic immunoglobulin was observed by immunofluorescence techniques. These findings suggest that, besides alpha-chain disease, Mediterranean lymphomas include other histological types of diffuse intestinal sarcomas. (21 refs.)

77-4111 **Vaccinia Necrosum Complicating Immunoblastic Sarcoma.** (Eng.) Turkel, S. B. (Dept. Pathology, Room 1M3, WH, Los Angeles County-Univ. Southern California Medical Center, 1200 N. State St., Los Angeles, CA 90033) Overturf, G. D. *Cancer* 40(1): 226-233; 1977.

The case history of a 59-yr-old man with immunoblastic lymphadenopathy that evolved over a 3-yr period into immunoblastic sarcoma is presented. The course was complicated by vaccinia necrosum following small pox vaccination. The persistence of the virus was diagnosed at autopsy. This case indicates the hazard of live viral vaccines to immune-compromised hosts. (16 refs.)

77-4112 **Familial Occurrence of Colon and Uterine Carcinoma and of Lymphoproliferative Malignancies. II. Chromosomal and Immunologic Abnormalities.** (Eng.) Law, I. P. (Hematology-Oncology Service, Womack Army Hosp., Fort Bragg, NC 28307) Hollinshead, A. C.; Whang-Peng, J.; Dean, J. H.; Oldham, R. K.; Herberman, R. B.; Rhode, M. C. *Cancer* 39(3): 1229-1256; 1977.

Cytogenic and immunologic studies were performed on 20 members of a family who had an increased susceptibility to carcinomas of the colon and uterus and to lymphoproliferative malignancy. Chromosomal abnormalities, such as small G and/or long submetacentric marker chromosome and other aberrations, were observed in members who had cancer and in some asymptomatic siblings. In addition, impairment of T-cell function was noted in many of the members, suggesting that defective cell-mediated immunity, which also may be genetically determined, played an important role in the expression of this disease. (29 refs.)

77-4113 **Pathological Study of Alpha-Chain Disease, with Special Emphasis on Evolution.** (Eng.) Galian, A. (Gastroenterology Clinic, Hopital Saint-Lazare, 107 Bis, rue du Faubourg Saint-Denis, 75475 Paris Cedex 10, France) Lecestre, M. J.; Scotto, J.; Bognel, C.; Matuchansky, C.; Rambaud, J. C. *Cancer* 39(5): 2081-2101; 1977.

A report is presented of the pathology, treatment, and evolution of alpha-chain disease (α-CD) in six patients, four of whom were followed until death or complete remission. In each organ involved, lesions could be classified into three histotopographical stages. Histological, immunofluorescent, and ultrastructural techniques indicated that Stage C is an immunoblastic sarcoma possibly derived from the same clone as the initial plasmacytic stage, Stage A. In Stage B, atypical plasma cells and immunoblastlike cells are located deep in the gut wall. Because of the diversity of lesions in the same patient at the same time, a laparotomy is required for accurate staging. Rectum, stomach, liver, and spleen localizations were observed at various times during evolution. Stage A patients had the best prognosis and responded well to antibiotics and chemotherapy, whereas those with Stage C had the poorest prognosis. Mediterranean lymphoma and α-CD share identical etiological, clinical, and pathological features. The frequency of α-CD protein synthesis in α-CD patients could be determined by immunochemical studies. (49 refs.)

77-4114 **Origin of Reed-Sternberg Cell (Letter to Editor).** (Eng.) Schmitt, D. (Laboratoire d'Immunopathologie, Clinique Dermatologique, Hopital Edouard Herriot, 69374 Lyon Cedex 2, France) Alario, A.; Perrot, H.; Thivolet, J. *Lancet* 2(8029): 137; 1977.

The absence of specific T and B cell markers on the surface of Reed-Sternberg cells suggests that they are not of lymphocytic origin. However, they could be monocytic in origin. (7 refs.)

77-4115 **An Ultrastructural Study of Hodgkin's Disease Suggesting a Mononuclear Phagocytic (Histiocytic) Origin of Reed-Sternberg and Lacuna Cells.** (Eng.) Henry, K. (Dept. Histopathology, Westminster Medical Sch., London, S.W.1., England) *IRCS Med Sci: Cancer* 5(7): 324-325; 1977.

The results of an ultrastructural study suggest that the characteristic Reed-Sternberg and lacuna cells of Hodgkin's disease are histiocytic. If this is true, the disease would represent a reaction of normal lymphocytes to a neoplasm of the mononuclear phagocyte system. (6 refs.)

77-4116 **Hodgkin's Disease in Children.** (Eng.) Smith, I. E. (Royal Marsden Hosp., Sutton, Surrey, England) Peckman, M. J.; McElwain, T. J.; Gazet, J. C.; Austin, D. E. *Br J Cancer* 36(1): 120-129; 1977.

A study of 59 children with Hodgkin's disease over a 34-yr period indicated an overall increased male incidence and an increased male incidence of lymphocyte-predominating histology. This disease is rare in children in Western countries. (23 refs.)

77-4117 **Growth of Cultured Cells from Patients with Hodgkin's Disease and Transplantation into Nude Mice.** (Eng.) Zamecnik, P. C. (John Collins Warren Labs., Huntington Memorial Hosp. Harvard Univ. at Massachusetts General Hosp., Boston, MA 02114) Long, J. C. *Proc Natl Acad Sci USA* 74(2): 754-758; 1977.

Long-term monolayer cell cultures were prepared from tumor nodules in spleens from 28 patients with Hodgkin's disease and from 84 normal adult or human fetal spleens and from fetal thymuses. After 5-20 serial passages in culture, cells from nine of the Hodgkin's disease monolayers underwent morphologic change in vitro with transition from a spindle and reticular pattern of replication to polygonal and round cells that propagated in mosaic arrays. Four of the monolayer cell lines were injected into 43 nude, athymic mice. In 36 animals, neoplasms developed at the inoculation site that were locally destructive, capable of pulmonary metastasis, and eventually fatal to the recipients. Transplanted tumors were not observed in 18 athymic mice inoculated with cultures prepared from normal human adult spleen and fetal spleen and thymus, nor were tumors seen in 16 animals that received fresh, noncultured Hodgkin's disease tumor tissue. On microscopic examination, xenografts derived from Hodgkin's disease cultures were pleomorphic malignant neoplasms composed of large, undifferentiated cells resembling reticulum cell sarcoma. These neoplasms did not involve the lymphoreticular organs of mice. Chromosome studies indicated that the transplanted neoplasms were composed of human cells with an aneuploid karyotype and that monolayer cultures prepared from the heterotransplants contained a karyotype similar to that of the cultured cells prior to passage in mice. The ability of these Hodgkin's disease cell lines to produce invasive tumors with human karyotypes in nude mice is evidence of the neoplastic nature of the monolayer cells and their relationship to the malignant cell of the human disorder. (15 refs.)

77-4118 **Spontaneous Lymphosarcoma Arising in a Nude Mouse: Characterization In Vivo and In Vitro.** (Eng.) Tralka, T. S. (Lab. Pathology, NCI, NIH, Public

Health Service, U.S. Dept. Health Education, and Welfare, Bethesda, MD 20014) Costa, J.; Sindelar, W. F.; Rabson, A.; Gullino, P. M.; Henson, E.; Chu, E. W.; O'Conor, G. T. *J Natl Cancer Inst* 58(4): 977-982; 1977.

A lymphosarcoma spontaneously arising in a nude mouse and a continuous cell line (NML-1) derived from it are described and compared. The primary tumor and a transplantable tumor line established from it were composed of lymphoid cells, with no C-type viral particles demonstrable by electron microscopy. The culture line was composed of cells with morphologic and functional properties of macrophages; budding C-type particles were abundant. Cells in the tumors produced in nude mice by injection of NML-1 cells also resembled macrophages rather than lymphocytes; however, the tumors lacked C particles. The findings suggest some type of in vivo suppression of complete virus expression. (21 refs.)

77-4119 **Clinical Correlation of a Biochemical Marker for Transformed Cells (Meeting Abstract).** (Eng.) Hampton, J. W. (Oklahoma Medical Res. Foundation, Oklahoma City, OK 73104) Weidenbach, A.; Radcliffe, R.; Rao, S.; Heinze, T. *Proc Am Assoc Cancer Res* 18: 306; 1977. (1 ref.)

77-4120 **Circulating Tumor Cells in Murine Myeloma.** (Eng.) Warner, T. F. (Dept. Special Hematology, Mayo Clinic, Rochester, MN 55901) Moses, H. L.; Fair, D. S.; Krueger, R. G. *J Natl Cancer Inst* 58(4): 983-992; 1977.

BALB/c mice bearing sc ADJ-PC5 myelomas had hematologic features suggestive of a preleukemic syndrome: thrombocytopenia, anemia, leukocytosis, and megakaryocytic hyperplasia. Six BALB/c myelomas (ADJ-PC5, FLOPC-1, MOPC-104E, MOPC-46B, MOPC-173D, and MOPC-21) were successfully transplanted sc by fragments or cell suspensions of spleens from mice with sc tumors, although typical myeloma cells were difficult to visualize by light microscopy in these spleens. The fidelity of transmission of the ADJ-PC5 myeloma by this procedure was shown by retention of the idiotypic specificity of the immunoglobulin produced by the tumor in a radioimmunoassay. Tumorigenic cells homed to the spleen as early as 8 days after myeloma transplantation. The spleens of tumor-bearing mice, however, could destroy or suppress the expansion or growth of a limited number of the migrant tumor cells. Tumorigenic cells in the peripheral circulation constituted 2%-3% of the WBC. These cells had reduced levels of murine myeloma viral and cell-associated antigens, were difficult to detect by indirect immunofluorescence, and did not divide rapidly, as indicated by the low number of cells detected by autoradiography. The nature and identity of the spleen-homing myeloma cells remain to be determined. (35 refs.)

See also:

* (Rev.): 77-3601, 77-3613, 77-3638, 77-3640, 77-3664, 77-3666, 77-3667, 77-3668, 77-3669, 77-3670, 77-3671, 77-3672, 77-3673, 77-3674, 77-3675, 77-3677, 77-3678, 77-3681, 77-3683, 77-3685, 77-3686, 77-3687, 77-3691, 77-3692, 77-3692, 77-3693, 77-3694, 77-3695, 77-3696.
* (Chem.): 77-3704, 77-3727, 77-3777, 77-3791, 77-3792, 77-3810, 77-3822, 77-3825.
* (Phys.): 77-3830, 77-3833, 77-3834, 77-3835, 77-3845, 77-3846, 77-3849, 77-3850.
* (Viral): 77-3860, 77-3890, 77-3892, 77-3909, 77-3951.
* (Immun.): 77-3971, 77-3972, 77-3973, 77-3975, 77-3976, 77-4007, 77-4017, 77-4019.
* (Epid.-Biom.): 77-4123, 77-4124, 77-4125, 77-4126, 77-4131, 77-4140, 77-4142, 77-4146, 77-4151, 77-4153.

EPIDEMIOLOGY AND BIOMETRY

77-4121 **Contribution of the Environment to Cancer Incidence: An Epidemiologic Exercise.** (Eng.) Wynder, E. L. (Div. Epidemiology, American Health Foundation, New York, NY 10019) Gori, G. B. *J Natl Cancer Inst* 58(4): 825-832; 1977.

To determine more precisely the influence of individual environmental causes of cancer, differences among population groups, sex ratios, time trends, and demographic and socioeconomic variables were investigated. Six tables of data show inter- and intracountry comparisons for major cancer types. The worldwide distribution of mortality rates for men illustrates the environmental influences on all cancer sites. The ratio between high- and low-risk rates is >2.0 for all cancers. Except for leukemia, the same is true for women. Intracountry differences can be ascribed to intensity of sunlight, industrialization, regional dietary habits, etc. Intracountry differences for stomach cancer usually involve higher rates in northern regions than in southern ones, as noted in Yugoslavia and the US. These geographic differences may be related to diet. The effect of environment is also indicated by the different rates for men and women of non-sex-linked cancers. Changes in cancer rates within a specific period of time can also help to pinpoint environmental factors. The increase in lung cancer incidence since 1930 is consistent with increased cigarette smoking, and the sharp decrease in stomach cancer suggests a decrease in an environmental factor or introduction of a dietary protective factor(s). Factors such as tobacco use, nutrition, air and water pollution, occupational exposure, and drugs are discussed individually. The percentage of cancer incidence in the US attributable to specific environmental factors (diet, tobacco, radiation, occupation, alcohol, exogenous hormones) is shown graphically. (66 refs.)

77-4122 **Why Do Human Cancer Death Rates Increase with Age? A New Method of Analysis of the Biology of Cancer.** (Eng.) Burton, A. C. (Dept. Biophysics, Univ. Western Ontario, London, Ontario N6A 5C1, Canada) *Perspect Biol Med* 20(3): 327-344; 1977.

A mathematical analysis, based on simple logic, of the increase in human cancer death rates with age is presented. The results seem to give a new perspective on the biology of human tumors. Data of the World Health Organization on the absolute numbers of male and female deaths in 1965 from cancer, in 5-yr age groups from birth >85 yr, were used. They included totals for all sites and for up to 50 specific sites from 37 countries. Cancer can be considered to start at some given time and then to require an incubation period before it causes death. The probability of a start may depend on age, described by a start function. The incubation period may be described by a lethality function of the period between start and the age at which death rates are measured. Differential curves of the death rate (dR) vs age (dA) must give the product of the start function x the lethality function. These curves, with the exception of the brain and CNS, strongly favor the random start theory and discount the senescence theory (except for the CNS) and suggest that the differential dR/dA gives the lethality curve for a particular tumor site. The start rate is independent of age (not $>3/1{,}000$ population/yr for the commonest tumors), and there is an extremely long incubation period of at least 20-50 yr. For most sites, the curves indicate that from 25% to 40% of the cancers do not cause death, as other causes supervene. Implications of these findings as to the possibilities of cancer control and to the relevance of experimental cancer research are discussed. (6 refs.)

77-4123 **Secular Trends of Cerebellar Gliomas in Children.** (Eng.) Fulchiero, A. (Dept. Neurology, Children's Hosp. Medical Center, 300 Longwood Ave., Boston, MA 02115) Winston, K.; Leviton, A.; Gilles, F. H. *J Natl Cancer Inst* 58(4): 839-843; 1977.

Temporal changes in the histologic composition of cerebellar gliomas were examined in a population of 132 children operated on between 1927 and 1968. Linear trends with time were examined for clinical features, histologic features, and tumor types. The percentage of children with glioma A and its histologic features (microcyst, leptomeningeal deposit, Rosenthal fiber, and focus of oligodendroglia) increased markedly over the 41-yr study period. This tumor is associated with a good prognosis. Glioma B, a tumor type associated with a poor prognosis, was relatively stable with respect to time. This tumor is associated with perivascular pseudorosette, calcification in the absence of glioma features, and high cell density, necrosis, or mitosis. The distribution of glioma A cases with oligodendroglial foci clustered by year of surgery within a relatively short time span. All 16 patients with the feature survived, and the male sex ratio was 0.81. For all other histologic features, the male sex ratio was between 0.43 and 0.63. (9 refs.)

77-4124 **Statistical Study on Malignant Melanoma in Japan (1970-1976).** (Eng.) Ohsumi, T. (Dept. Dermatology, Iwaki Kyoritsu Hosp., Iwaki, Japan) Seiji, M. *Tohoku J Exp Med* 121(4): 355-364; 1977.

A statistical study of the 456 cases of melanoma diagnosed in Japan from 1970 to 1976 confirmed the trends identified in a previous study of 501 cases diagnosed between 1961 and 1970. The yearly incidence of melanoma is increasing, with the av number of patients being 71.1/yr. The age distribution shows a peak in the seventh decade, and the incidence is slightly higher in men than in women (1.1:1). The incidence by age/10,000 population increases during the fifth decade and shows two peaks, in the seventh and eighth decades. The av age at onset of all melanoma is 51.6 yr, but the av age at onset of brain and spinal cord melanoma is 25.4 yr. In patients with preexisting skin lesions at sites other than the foot, the av age at onset of melanoma is 38.7 yr; the av age of patients with melanoma of the foot is 65.9 yr. The incidence of melanoma of the sole is high (51%) in relation to the number of melanocytes per unit area of skin. The incidence of metastatic melanoma of the eye is low (23%). (12 refs.)

77-4125 **Frequency and Significance of Bone Marrow Involvement by Metastatic Solid Tumors.** (Eng.) Anner, R. M. (Dept. Lab. Medicine, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX 77030) Drewinko, B. *Cancer* 39(3): 1337-1344; 1977.

A total of 3,620 bone marrow aspirates from 2,877 patients with solid tumors were evaluated for the presence of clinically unsuspected metastasis. All aspirates were obtained from the iliac crest as part of the prechemotherapy workup and processed as smear and paraffin sections of the clot. Of the 2,877 patients, 263 showed metastatic tumor. Of these, metastasis was most frequent in neuroblastoma (48.2%), Ewing's sarcoma (35.5%), oat cell carcinoma (20.7%), prostate carcinoma (20.3%), breast carcinoma (19.6%), squamous cell carcinoma of the lung (15.7%), rhabdomyosarcoma (16.2%), and melanoma (6.8%). In most instances (92%), tumor cells were demonstrated simultaneously on both smears and clot sections. However, in lung and breast carcinoma, metastasis was noted more frequently in clot sections, but smears were superior for detecting neuroblastoma and rhabdomyosarcoma. The prognostic significance of bone marrow involvement in 83 patients with Stage IV malignant melanoma scheduled for immunochemotherapy was investigated. In 39 patients (Group B, no bone marrow infiltration), the median survival was 59 wk. In 44 patients (Group A, infiltrated bone marrow), the median survival was 6 wk. Although bone marrow metastasis did not preclude response to immunochemotherapy, after 40 wk only two Group A patients were still alive, compared with 16 in Group B. This study demonstrates the usefulness of combining clot section and smear examinations for increased detection of unsuspected bone marrow metastasis and suggests the prognostic significance of bone marrow involvement in malignant melanoma. (13 refs.)

77-4126 **The Changing Incidence of Association of Hepatitis B with Hepatocellular Carcinoma in California.** (Eng.) Peters, R. L. (Dept. Pathology, John Wesley Hosp., 2826 S. Hope St., Los Angeles, CA 90007) Afroudakis, A. P.; Tatter, D. *Am J Clin Pathol* 68(1): 1-7; 1977.

Liver specimens from 168 patients who had died of hepatocellular carcinoma and were autopsied from 1949 through 1974 were examined for hepatitis B surface antigen (HBsAg) by two staining methods, Shikata's orcein and peroxidase-antiperoxidase. HBsAg was demonstrated in 21% of the patients in whom hepatocellular carcinomas arose in preexisting chronic hepatic disease. Of 39 patients who had carcinomas arising in essentially normal livers, only 1/19 tested had HBsAg: that 1 patient was an iv drug user. Both the total number of hepatic cancers and the percentages that were HBsAg-positive increased beginning in 1970; the numbers of hepatocellular carcinomas arising in noncirrhotic livers also increased. In 1969-1974, 73% of those who had hepatocellular carcinomas arising in nonalcoholic but cirrhotic livers were HBsAg-positive. Certain racial differences were identified in the series that probably result from different life styles. Whether the increasing incidence of HBsAg positivity reflects shifts in population groups or the sequel of an earlier epidemic of hepatitis B is unclear. If the increase of HBsAg-positive hepatocellular carcinomas reflects a previous hepatitis B epidemic, a similar peak may result from the hepatitis B epidemic in the US that coincided with the popularity of iv drug use. (28 refs.)

77-4127 **Epidemiology of Malignant Neoplasms in the German Democratic Republic From 1962 to 1972.** (Ger.) Schott, J. (Lehrstuhl fur Soziale Gynakologie des Bereiches Medizin-Charite, DDR-104 Berlin, Tucholskystrasse 2, E. Germany) *Arch Geschwulstforsch* 47(1): 45-56; 1977.

The epidemiology of malignant neoplasms in the German Democratic Republic (GDR) from 1962 to 1972 is surveyed. During this period, 400,000 cases of cancer per 17 million total population occurred. All patients were followed over their lifetime. Recurrences were not included in the total. The sex distribution was about equal; however, the 5-yr survival rate was 39% for women, 14% for men. Other than the fact that the prognosis is better for women than for men, no explanation for this difference is presented. Demographic charts and tables are given for malignancies numbers 140-209 (not identified), as listed in the 8th Revision of the Classification of Disease". Difficulties and errors in the interpretation of the data are discussed. (12 refs.)

77-4128 **Epidemiology and Histopathology of Hodgkin's Disease in Finland.** (Eng.) Franssila, K. O. (Div.

Surgical Pathology, Barnes Hosp., Barnes Hosp. Plaza, St. Louis, MO 63110) Heiskala, M. K.; Heiskala, H. J. *Cancer* 39(3): 1280-1288; 1977.

All 314 cases diagnosed as Hodgkin's disease (HD) in Finland from 1961 to 1964 were histologically reexamined and reclassified. After reexamination, only 207 cases were regarded as HD. The age-specific incidence curve of HD both before and after reexamination was bimodal. The second peak was much lower in the reexamined series because of the exclusion of many non-Hodgkin's lymphomas. The bimodality was more clear in women. Hodgkin's disease was more common in urban than in rural areas. This difference was greatest in young adults. Nodular sclerosis (NS) was the most common histologic type (53% in men, 83% in women). Its age-specific incidence curve was bimodal, with a higher peak in young adults. It was more common in urban areas and occurred there at younger age than in rural areas. Lymphocytic predominance, mixed cellularity, and lymphocytic depletion groups had the highest incidence rates in old age. HS seems to be composed of two or more entities, one of which is the young adult disease, probably the most common entity in western countries, especially in urban areas. The entities do not correspond strictly to the present histologic types. However, most cases of NS probably represent young adult disease and most patients with young adult disease have NS. (29 refs.)

77-4129 **Epidemiology of Non-Hodgkin's Lymphoma.** (Ger.) Tulinius, H. (Krabbameinsska, Icelandic Cancer Registry, Krabbamienstelag Islands, Suclurgata 22-24, Box 523, Reykjavik, Iceland) *Strahlentherapie* 153(4): 209-217; 1977.

The main sources for this statistical study of the epidemiology and mortality of non-Hodgkin's lymphomas (NHL) were cancer registries and the mortality statistics of the World Health Organization. Some information was also obtained from pathology institutes and hospitals. Mortality from NHL varies from 1/100,000 in Thailand to 6.2/100,000 in Israel. Incidence of NHL varies from 1.0/100,000 in Poland to 10/10,000 in Israel. Men are affected with NHL twice as often as women. The high incidence of NHL in Israel can be attributed to the frequent occurrence of intestinal lymphomas in the eastern Mediterranean area. A similar high incidence in Nigeria is based on the large number of Burkitt's lymphoma cases in this country. Overall, most NHL are either lymphosarcomas or reticulum cell sarcomas. Of the total NHL in patients aged <20 yr, the number of lymphosarcomas varies from 5% in Nigeria to 58% in Norway. Reticulum cell carcinomas vary from 0% in Peru and Norway to 30% in Brazil. Lymphogranulomas vary from 8% in Nigeria to 70% in Egypt. The distribution is similar for the age group 20-49 yr. For patients >50 yr, lymphosarcomas vary from 15% in Japan to 50% in Brazil. Reticulum cell carcinomas vary from 8% in Brazil to 61% in Egypt. A correlation may be found between the high percentages of certain lymphomas and other viral and infectious diseases. (24 refs.)

77-4130 **A Cohort Analysis of Pancreatic Cancer, 1939-1969.** (Eng.) Benarde, M. A. (Dept. Community Medicine and Environmental Health, Hahnemann Medical Coll. and Hosp., Philadelphia, PA 19102) Weiss, W. *Cancer* 39(3): 1260-1263; 1977.

Pancreatic cancer mortality in the US was examined by cohort analysis for the period 1939 to 1969. Birth controls at 5-yr intervals were studied. White men and nonwhites of both sexes showed a shift of the cohort mortality rate curves by age toward younger groups as birth cohorts went from 1870-1874 to 1900-1904. This shift disappeared in white men and diminished in nonwhites of both sexes between the cohorts of 1890-1894 and 1900-1904. The shift in nonwhites was larger than that in white men, so that although nonwhites had lower rates than whites in earlier birth cohorts, their rates exceeded those of whites in the most recent cohort. In the search for environmental cause(s) of pancreatic cancer, exposure characteristics should be compatible with these observations. (19 refs.)

77-4131 **Prophylactic Gynecologic Examinations During Inpatient Care.** (Ger.) Flach, W. (Frauenklinik des Stadtischen Klinikums Berlin-Buch, DDR-1115 Berlin, Wiltbergstrasse 50, E. Germany) Buchner, C.; Pressler, H. *Zentralbl Gynaekol* 99(7): 422-428; 1977.

Of 2,960 inpatients who were screened at 26 specialty clinics in East Germany, 2,047 were gynecologically healthy, 847 had benign gynecologic diseases, 56 had histologically confirmed tumors (including 5 carcinomas in situ, 3 microcarcinomas, and 3 cervical carcinomas, Stage Ib and higher), and 10 had suspected, but histologically unconfirmed, malignancies. (16 refs.)

77-4132 **Can the Search for Early Stages of Cancer of the Cervix Uteri Be Improved? An Empirical and Theoretical Study of Medical Sociology.** (Ger.) Pauli, H. K. (Universitats-Frauenklinik Erlangen-Nurnberg, Universitatsstrasse 21/23, D-8520 Erlangen, W. Germany) Trotnow, S. *Arch Gynaekol* 222(2): 159-186; 1977.

Using a standardized questionnaire, 7,356 patients (30 yr and older) were interviewed. Women with cervical cancer or precancerous stages were compared with the remaining patients. Sociological factors in both groups were weighed against each other. A higher risk of cervical cancer was found in women that were widowed, divorced, or separated and in women with less social contact, less education, lower social standing, lower standards of personal hygiene, earlier age at first coitus, more sexual partners, lower age at first delivery, and more deliveries. Combination of two or more of these sociological factors increases the risk of cervical cancer. Most of the women in the high-risk groups had fewer annual checkups. As a result, a higher incidence of cervical cancer is to be expected in the 70% of women >30 yr old who do not have annual examinations compared to the 30% who do. (38 refs.)

77-4133 **Recent Results from the British Columbia Screening Program for Cervical Cancer.** (Eng.) Boyes, D. A. (Cytology Lab., Cancer Control Agency British Columbia, 2656 Heather St., Vancouver 9, British Columbia, Canada) Nichols, T. M.; Millner, A. M.; Worth, A. J. *Am J Obstet Gynecol* 128(6): 692-693; 1977.

Data from the British Columbia screening program for cervical cancer show that the incidence of invasive squamous carcinomas has decreased steadily since 1955 (28.4/100,000) and is now 8.6/100,000 women over age 20. The current mortality rate is 4.8/100,000, as opposed to 11/100,000 in 1955. (3 refs.)

77-4134 **Hormonal Status of Cervical Cancer.** (Eng.) Kodama, M. (Lab. Chemotherapy, Aichi Cancer Center Res. Inst., Chikusa-ku, Nagoya, Japan) Kodama, T.; Totani, R. *J Natl Cancer Inst* 59(1): 41-47; 1977.

The urinary steroid profiles of 201 patients with cervical cancer were investigated by gas-liquid chromatography. Of the 14 identified neutral steroids, urinary levels of all but 1 (tetrahydrocortisol) were reduced in premenopausal cancer patients compared with premenopausal controls. The extent of steroid deficiencies did not parallel the progress of neoplasia, but it was comparable to that of the postmenopausal controls. Urinary levels of androsterone and 11-ketoandrosterone were significantly lower in postmenopausal patients than in the corresponding controls. Evidence indicated that ovulation in a premenopausal patient proceeds normally despite reduced excretion of all menstruation-dependent steroids (11-hydroxyandrosterone, 11-hydroxyetiocholanolone, pregnanediol, and pregnanetriol). Patients with cervical cancer did not differ significantly from controls with regard to the number of live births. More 20- to 50-yr-old women with cervical cancer had delayed menstrual cycles than did breast cancer patients, indicating an abnormal function of the hypothalamus-pituitary axis. Changes in urinary steroids suggest some developmental disturbance in the genesis of cervical cancer. (21 refs.)

77-4135 **Hormonal Status of Breast Cancer. III. Further Analysis of Ovarian-Adrenal Dysfunction.** (Eng.) Kodama, M. (Lab. Chemotherapy, Aichi Cancer Center Res. Inst., Chikusa-ku, Nagoya, Japan) Kodama, T.; Miura, S.; Yoshida, M. *J Natl Cancer Inst* 59(1): 49-54; 1977.

Detailed studies of urinary steroids in patients with breast cancer and normal controls showed that abnormal aging processes and depressed corpus luteum function are associated with this form of cancer. The ratio of androsterone to tetrahydrocortisol, an index of the aging process, was significantly lower in 157 breast cancer patients than in 247 normal pre- and postmenopausal women. In premenopausal women, the ratio decreased in the order of rural controls, urban controls, and patients with breast cancer. Apart from a general depression of menstruation-dependent steroids, breast cancer was associated with disproportionately low excretions of pregnanediol and pregnanetriol within the menstruation-dependent steroid family. The belief that this reflects the delay or complete failure of ovulation was supported by the reduced parturition rate of the breast cancer patients compared with the controls. The possibility that steroidal deviations in breast cancer are related to abnormal functioning of the hypothalamus-pituitary axis is discussed. (13 refs.)

77-4136 **Epidemiology of Breast Cancer in Alberta 1971-1973 (Meeting Abstract).** (Eng.) Lees, A. W. (Dr. W. W. Cross Cancer Inst., Edmonton, Alberta, Canada T6G 1Z2) Bako, G. *Proc Am Assoc Cancer Res* 18: 325; 1977. (no refs.)

77-4137 **Benign and Malignant Female Breast Disease in Northern Alberta, 1971-1974 (Meeting Abstract).** (Eng.) Burns, P. E. (Dr. W. W. Cross Cancer Inst., Edmonton, Alberta, Canada) May, C.; Grace, M. G. *Proc Am Assoc Cancer Res* 18: 297; 1977. (no refs.)

77-4138 **Relationship Between Steroid Excretion Patterns and Breast Cancer Incidence in Israeli Women of Various Origins.** (Eng.) Gross, J. (Experimental Medicine and Cancer Res., Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel) Modan, B.; Bertini, B.; Spira, O.; de Waard, F.; Thijssen, J. H.; Vestergaard, P. *J Natl Cancer Inst* 59(1): 7-11; 1977.

A random survey of 300 postmenopausal Israeli women of European, North African, Middle Eastern, or Yemenite origin demonstrated differences between high- and low-risk groups for breast cancer with respect to age at first parturition, number of pregnancies, number of live births, height, and wt. The direction of the differences was in line with that observed for breast cancer patients. The groups also differed in the excretion of estriol, 17-ketosteroids, and allotetrahydrocortisol. Multiple regression analysis revealed that estriol excretion was significantly lower in population groups with a high incidence of breast cancer (European, North African). This trend, which has also been observed in adolescent and premenopausal women, may reflect environmental influences on peripheral estrogen metabolism. (37 refs.)

77-4139 **Geographic Variation in the Occurrence of Cancer in Thailand Compared with Other Countries** (Meeting Abstract). (Eng.) Boonyanit, S. (Dept. Pathology, Sch. Medicine, Univ. Maryland, Baltimore, MD) Kaiser, H. E. *Proc Am Assoc Cancer Res* 18: 182; 1977. (no refs.)

77-4140 **Carcinoma of the Gallbladder in a Population of Southwestern American Indians.** (Eng.) Black, W. C. (Cancer Res. and Treatment Center, Univ. New Mexico, 900 Camino De Salud, NE, Albuquerque, NM 87131) Key, C. R.; Carmany, T. B.; Herman, D. *Cancer* 39(3): 1267-1279; 1977.

The New Mexico Tumor Registry was used as a case-finding source in assessing the clinicopathological characteristics of gallbladder carcinoma in a group of 56 Southwestern American Indian patients. According to the registry this is the third most common malignant tumor among American Indian women, accounting for 8.5% of specific cancer diagnoses by site. Gallbladder carcinoma is more common within the Indian population than among Spanish Americans or Anglos living in this area. This is true for both sexes. No significant differences in av age at diagnosis, ratio of female to male patients, signs and symptoms, stage at diagnosis, or survival were detected in comparison with studies pertaining to gallbladder carcinoma in non-Indian populations. A squamous cell carcinoma component was unusually common, however, and carcinoma in situ or atypical adenomatous hyperplasia of the mucosa was frequently documented adjacent to invasive carcinoma. Although gallstones were present in tumor-containing gallbladders in 93% of cases, elective cholecystectomy for cholelithiasis is probably not a practical means of tumor prevention in view of the unusual frequency of cholelithiasis in Indian women. Pharmacological conversion of bile to a nonlithogenic form may deserve consideration as prophylaxis against both cholelithiasis and gallbladder carcinoma in this population. (72 refs.)

77-4141 **Food and Diseases.** (Eng.) Knox, E. G. (Health Services Res. Centre, Birmingham, England) *Br J Prev Soc Med* 31(2): 71-80; 1977.

Statistical correlations between the main foodstuff and nutrient intakes and the chief causes of mortality in 17 European countries and in Canada, US, and Japan were examined. Subsidiary examinations were made of the effects of including and excluding Japan and of the effects of various statistical standardization procedures. Complex food patterns were identified and related both to geographical latitude and to levels of affluence; these, in turn, were related to complex patterns of mortality. Criteria for drawing special attention to specific associations were identified, based partly on statistical significance tests and also on strength-of-association yardsticks supplied by diseases with known causes. Findings suggesting causal interpretations were (1) alcohol intakes and cirrhosis of the liver, cancer of the mouth, and cancer of the larynx; (2) total fat intakes and multiple sclerosis, cancer of the large intestine, and cancer of the breast; and (3) beer and cancer of the rectum. (25 refs.)

77-4142 **Malignant Thyroid Tumors Before and After the Introduction of Iodine Prophylaxis.** (Ger.) Bubenhofer, R. (Institut fur Pathologie, Universitat Zurich, Kantonsspital, CH-8091 Zurich, Switzerland) Hedinger, C. *Schweiz Med Wochenschr* 107(21): 733-741; 1977.

Switzerland, once an area of endemic goiter, introduced iodine supplementation of table salt into a few cantons in 1923. This practice later became widespread along with the consumption of imported foods. The records and tissues of two periods, 1925-1941 and 1962-1973, were reexamined to determine the effect of iodine prophylaxis on the relative incidence of certain tumor types. The malignant tumors of the earlier period were reexamined and reclassified according to 1974 WHO nomenclature. Of 268 thyroid malignancies biopsied during the first period, there were 112 follicular, 99 anaplastic, and 21 papillary carcinomas, and 36 miscellaneous tumors. In comparison, of 327 cases examined from the second period, there were 97 follicular, 78 anaplastic and 109 papillary carcinomas, and 43 miscellaneous tumors. The proportion of differentiated carcinomas has increased from 1962 onward. The ratio of men:women has also changed, from 1:1.3 in the first period to 1:2.1 in the second. (45 refs.)

77-4143 **Epidemiology of Gastric and Colo-rectal Cancer in the United States and Chile with Particular Reference to the Role of Dietary and Nutritional Variables, Nitrate Fertilizer Pollution, and N-Nitroso Compounds.** (Eng.) Zaldivar, R. (2170 N.W. 11th St., Suite 53, Miami, FL 33125) *Zentralbl Bakteriol [Orig B]* 64(3): 193-217; 1977.

An epidemiological investigation was conducted of (1) infant and general mortality rates in the period 1930-1970; (2) age curve and sex ratio of stomach cancer; (3) decline of stomach cancer mortality; (4) consumption of major food items, proteins, carbohydrates, fats, minerals, and vitamins; (5) correlation between food item consumption and gastric and colorectal cancer death rates; (6) statistical association between nitrate fertilizer exposure and gastric cancer mortality; and (7) statistical association between nitrate fertilizer soil pollution and stomach cancer death rates. The annual change in gastric cancer mortality rates, computed by linear regression, showed negative slopes for Chileans of both sexes. Each age group exhibited highly statistically significant p values ($p < 0.00005$) for gastric cancer mortality, except the male groups aged 65-74 yr. In Chile, from 1926-1927 to 1963-1967, the percent changes in the consumption of milk (+69.7), fats (+64.5), fish (+57.1), sugar (+41.2), and animal proteins (+34.4) were the most important ones. The marked decline in gastric cancer mortality was negatively associated with milk, animal protein, sugar, fish, and fat intake. The increase of colorectal cancer mortality was positively correlated with milk, sugar, animal protein, and fat intake. In the US, from 1963 to 1967, the daily consumption of animal proteins was 66 g (Chile 28.2 g), fats 147 g (Chile 41 g), and carbohydrates 372 g (Chile 543 g). In the US, the greatest percent changes (1910-1970) in nutrients were animal proteins (+34.6), vegetable proteins (-40.0), carbohydrates (-29.3), and riboflavin (+29.1). Exposure to nitrate fertilizers ($NaNO_3$ and KNO_3) was positively and significantly correlated in Chile with age-adjusted death rates/100,000 population for stomach cancer by province. (99 refs.)

77-4144 **Dietary Fibre, Transit-Time, Faecal Bacteria, Steroids, and Colon Cancer in Two Scandinavian Populations: Report from the International Agency for Research on Cancer Intestinal Microecology Group.** (Eng.) MacLennan, R. (International Agency Res. Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 2, France) IARC Working Group *Lancet* 2(8031): 207-211; 1977.

The dietary intake and fecal characteristics in population samples from two areas of Denmark and Finland with a fourfold variation in colon cancer incidence were compared. The study indicates that the etiology of colon cancer may be multifactorial and not associated in a simple manner with dietary fat, neutral steroids, acid steroids, or their bacterial metabolites. However, meat consumption was greater in the high-incidence areas. Higher intakes of dietary fiber and milk in the low-incidence area suggest a possible protective effect, unrelated to mouth-anus transit time. Further careful dietary and metabolic studies are needed to clarify the relationships between possible carcinogenic and protective effects of diet. (27 refs.)

77-4145 **Distribution of Small Bowel Tumors.** (Eng.) Lowenfels, A. B. (Div. Surgery, Westchester County Medical Center, Valhalla, NY 10595) Sonni, A. *Cancer Lett (Amsterdam)* 3(1/2): 83-86; 1977.

The anatomic distribution of 784 tumors of the small intestine was studied, and epidemiological data analyzed to determine the relation of these rare cancers to other gastrointestinal tumors and to diet. The anatomic distribution of cancer of the small intestine is unusual. Most tumors occur in the duodenum or proximal jejunum; relatively few tumors develop in the central bowel, and only in the lower ileum does the expected number of tumors appear. Available epidemiologic data show a correlation between small intestine cancer and lower, but not upper, gastrointestinal cancer. The incidence of small intestine cancer is positively correlated with protein and fat consumption. (9 refs.)

77-4146 **Comparative Histological Study of Large Bowel Adenomas in Japan and England with Special Reference to Malignant Potential.** (Jpn.) Muto, T. (Dept. Surgery, Univ. Tokyo, Tokyo, Japan) Ishikawa, K.; Kino, I.; Nakamura, K.; Sugano, H.; Morson, B. C.; Bussey, H. J. *Jpn J Cancer Clin* 23(5): 465-468; 1977.

In Japan and England, the malignant potential of adenomas of the large intestine varies with size, histologic type, and grade of epithelial dysplasia. Adenomas in Japan have a lower malignant potential than those in England, as reflected by the lower incidence of both large adenomas and villous adenomas. Since the adenoma-cancer sequence appears to occur in the same way in both countries, the lower incidence of colorectal cancer in Japan may be due to the lower prevalence as well as the smaller size of the Japanese adenomas. (13 refs.)

77-4147 **Lung Cancer in Hong Kong Chinese: Mortality and Histological Types, 1960-1972.** (Eng.) Chan, W. C. (Dept. Pathology, Univ. Hong Kong, Hong Kong) MacLennan, R. *Br J Cancer* 35(2): 226-231; 1977.

From 1960 to 1972, the age-adjusted mortality from lung cancer in Hong Kong increased 82.5% in men and 77.2% in women. The relative frequency of epidermoid carcinoma increased in male bronchial biopsies but not in lung biopsies, resections, or autopsies; the proportion of small cell anaplastic carcinomas declined in both sexes. Despite the rise in lung cancer mortality, the ratio of Kreyberg Group I tumors (epidermoid and small cell anaplastic) to Group II tumors (adenocarcinoma and carcinoid) declined in each sex during the 13-yr period. Adenocarcinoma was the most common tumor in women in spite of the high lung cancer mortality. It is suggested that cigarette smoking produces a different pattern of histological types among the Hong Kong Chinese or that additional etiologic factors are operating there. (12 refs.)

77-4148 **Epidemiology of Lung Cancer in England and Wales.** (Eng.) Waterhouse, J. A. (Birmingham Cancer Registry, Queen Elizabeth Medical Center, Birmingham B15 2TH, England) *IARC Sci Pub* (16): 229-240; 1977.

The UK lung cancer mortality rates were examined by geographical location, urban/rural areas, social class, and occupation. There is no overall trend in the rates for men in most of the standard geographical regions over the period 1953-1973, except in the north and in the rural sections of Wales. The variability in rate for women is even greater, making trends more difficult to discern. There is a clear division in incidence rates between urban and rural areas, all of the urban areas having higher rates than the rural sections of the same standard geographical region. When standardized mortality ratios for 1930-1932 are compared, no clear trend in lung cancer mortality incidence can be seen in either sex by social class in 1931, but by 1961 the trend is apparent, with low rates in social classes I and II (professional and upper-management classes) and high rates in class V (unskilled workers). Several occupational groups also show marked excesses in mortality from lung cancer. Highest among these are laborers (not otherwise classified), painters and decorators, and furnace, forge, foundry, and rolling-mill workers. Lowest rates are seen in professional and technical workers, artists, administrators and managers, farmers, foresters, and fishermen. (6 refs.)

77-4149 **The Philadelphia Pulmonary Neoplasm Research Project: The Risk of Lung Cancer in Relation to Symptoms and Roentgenographic Abnormalities.** (Eng.) Boucot, K. R. (Medical Coll. Pennsylvania, Philadelphia, PA 19129) Seidman, H.; Weiss, W. *Environ Res* 13(3): 451-469; 1977.

The presence or absence of several symptoms was recorded for a cohort of 6,027 male volunteers, aged 45 yr or older, who were screened by 70-mm photofluorography of the chest semiannually for 10 yr starting in 1951. The symptoms were persistent cough, worsening cough, expectoration, hemoptysis, heaviness or pain in the chest, unilateral or bilateral wheezing, hoarseness, and dyspnea. Smoking habits, wt, and height were also noted. Upon entry, 59% of the men had one or more symptoms. After adjustment for age, race, and smoking habits, the 10-yr probability of lung cancer was 2.41%, 2.64% for symptomatic men and 1.78% for asymptomatic men. Chronic cough and hoarseness were associated with increased risks of 2.98% and 3.42%, respectively. Coughing smokers who had smoked more than one pack a day for $\geq$ 40 yr had an incidence of 8.81%; noncoughing smokers also had a very high risk of 7.45%. Cancer risk was increased when the lung fields in chest x-rays suggested nonspecific disease. Thus, older men with chronic cough, hoarseness, and/or nonspecific radiographic abnormalities are suitable populations for surveillance for lung cancer development. (31 refs.)

77-4150 **Origin of Carcinoma of the Bronchus. Part I: The Smoking Hypothesis.** (Eng.) Dijkstra, B. K. (284 Hillside, Lynnwood, Pretoria, S. Africa) *S Afr Cancer Bull* 21(1): 7-16; 1977.

The widely accepted finding that cigarette smoking is correlated with an increased risk of lung cancer development is criticized as being based on inaccurate and contradictory data. Several errors in the data upon which the finding was based are discussed. (27 refs.)

77-4151 **Origin of Carcinoma of the Bronchus. Part II: The Time Hypothesis.** (Eng.) Dijkstra, B. K. (284 Hillside, Lynnwood, Pretoria, S. Africa) *S Afr Cancer Bull* 21(1): 17-24; 1977.

Evidence that the risk of lung cancer development is correlated to season of birth is discussed. In the northern part of the Netherlands, people born in March have twice as great a chance of getting lung cancer as those born in the summer months; for England and East Germany, these differences were found for other seasons. This phenomenon may be related to seasonal variations in vitamin A availability. (62 refs.)

77-4152 **Air Pollution and Asbestos Carcinogenesis: Investigation of Possible Synergism.** (Eng.) Selikoff, I. J. (Mount Sinai Sch. Medicine, City Univ. New York, Fifth Ave. and 100th St., New York, NY 10029) *IARC Sci Pub* 16: 247-253; 1977.

Studies on lung cancer in asbestos workers and in the general population are reviewed, and an approach to determining whether urban air pollution might augment the carcinogenicity of asbestos is discussed. Analysis of the mortality data for asbestos insulation workers indicated that their lung cancer death rate was extraordinarily high, but that the excess deaths were limited to workers who also had a history of cigarette smoking. The results of a prospective epidemiological investigation in 1959-1960 of $>$ 1 million men and women from countries of all sizes and types do not appear to indicate that general air pollution by itself significantly increases the risk of lung cancer. A prospective epidemiological study is now underway using 11,509 asbestos workers in the US and Canada, air pollution figures for 84 cities in which some of the union locals are located, and information on cigarette smoking. Of the 11,509 asbestos workers, 301 died of lung cancer, 312 of other malignant neoplasms, and 109 of asbestosis from 1967 through 1974. Studies are being conducted to determine whether there are variations in the ratios between observed and expected numbers of deaths in various mortality categories and whether these variations will show any consistent pattern in relation to concentrations of air pollutants in the cities concerned. (8 refs.)

77-4153 **Mesothelioma and Asbestos. A Socioprofessional Study of 54 Diffuse Pleural Mesotheliomas.** (Fre.) Gaucher, P. (Inspection Medicale du Travail, Nantes, France) de Lajartre, M. *Arch Mal Prof* 38(1/2): 274-276; 1977.

The case histories, since 1956, of 54 industrial workers (2 women, 52 men aged 37-77 yr) with diagnosed diffuse pleural mesotheliomas are reviewed. The majority worked in naval yards. None of the patients showed signs of pulmonary fibrosis upon x-ray, and only four showed pleural calcifications. Fibrohyaline plaques were observed in eight patients upon thoracotomy or autopsy. The presence of asbestos fibers in surgical samples was positive in 27/28 cases. Evidently, there is a relationship between asbestos fibers and pleural mesotheliomas. Inadequate record keeping and the lack of important occupational data on industrial workers are discussed. It is recommended that more adequate records be kept on all industrial workers. (no refs.)

77-4154 **Thymidine Labeling Index of Human Breast Carcinoma: Enhancement of In Vitro Labeling by 5-Fluorouracil and 5-Fluoro-2′-deoxyuridine.** (Eng.) Meyer, J. S. (Dept. Pathology, Jewish Hosp., 216 S. Kingshighway, St. Louis, MO 63110) Facher, R. *Cancer* 39(6): 2524-2532; 1977.

Two inhibitors of thymidylate synthetase, 5-fluoro-2′-deoxyuridine (FUdR) and 5-fluorouracil (FU), enhanced the in vitro thymidine labeling index (TLI) of human breast carcinoma cells by increasing the detectability of labeled nuclei in autoradiographs of S-phase cells. The TLI was measured with FU or FUdR enhancement in primary breast carcinomas from 9 women < 50 yr old. The mean age and geometric mean TLI were 8.0 and 6.3, respectively, for the younger group and 4.0 and 2.8, respectively, for the older group. Similar significant age-associated differences were noted in a series of 133 TLI measurements without FU or FUdR. The TLI was not significantly correlated with primary breast carcinoma size or number of axillary nodal metastases. The capacity to form axillary metastases must be related to factors other than the rate of cell replication in breast tumors. (21 refs.)

See also:

* (Rev.): 77-3601, 77-3602, 77-3603, 77-3607, 77-3610, 77-3611, 77-3614, 77-3615, 77-3620, 77-3621, 77-3622, 77-3624, 77-3634, 77-3636, 77-3641, 77-3642, 77-3643, 77-3671, 77-3672, 77-3677, 77-3678, 77-3680, 77-3681, 77-3682, 77-3683, 77-3696, 77-3697, 77-3698, 77-3700, 77-3702.
* (Chem.): 77-3738, 77-3810, 77-3822, 77-3823.
* (Phys.): 77-3820, 77-3844.
* (Viral): 77-3896.
* (Immun.): 77-4006.
* (Path.): 77-4056, 77-4057, 77-4059, 77-4073, 77-4081.

77-4155 **Serum Prolactin Concentrations Throughout the Menstrual Cycle of Normal Women and Patients with Recent Breast Cancer.** (Eng.) Cole, E. N. (Dept. Surgery, Univ. Hosp. S. Manchester, Withington Hosp., Manchester, M20 8LR, England) England, P. C.; Sellwood, R. A.; Griffiths, K. *Eur J Cancer* 13(7): 677-684; 1977.

Prolactin concentration was estimated by radioimmunoassay of serum samples taken daily throughout the menstrual cycle of 11 patients who had undergone mastectomy for primary breast cancer and 32 normal women. Although there were no marked cyclical changes in prolactin levels, concentrations were lowest in the follicular phase. Thus, comparison of normal and cancer subjects required detailed statistical analysis of the results from comparable stages of the monthly cycle. Midcycle peaks of estradiol and follicle-stimulating hormone and the onset of menstrual bleeding were used as reference points. Prolactin concentrations were similar in samples from normal and cancer groups, although some significant differences were found at certain stages of the cycle: on the fifth day preceding the midcycle estradiol peak, during the follicular and periovulatory phases, and among the highest midcycle levels. At these stages of the cycle, samples from the breast cancer patients had a greater prolactin concentration than normal controls, although levels were within the normal range. The physiological relevance of these higher prolactin concentrations is uncertain and, in general, this study clearly indicates little difference between serum prolactin levels in normal women and in breast cancer patients whose primary tumor had been removed $>$ 3 mo previously. (27 refs.)

77-4156 **Insulin-induced Growth Hormone Response in Patients with Uterus Carcinoma. I. Endometrial Carcinoma.** (Eng.) Madajewicz, S. (Dept. Thoracic Surgery, Roswell Park Memorial Inst., Buffalo, NY 14203) Haruppa, J.; Kaminska, J. *Eur J Cancer* 13(8): 801-804; 1977.

The insulin-induced growth hormone responses in 37 women with endometrial carcinoma were significantly lower than those in 11 healthy obese women. It is suggested that the capacity of growth hormone receptors may be increased in breast cancer. The role of the hormone in endometrial carcinoma is unclear. (13 refs.)

77-4157 **Progesterone and Progesterone Receptors in Experimental Breast Cancer.** (Eng.) Horwitz, K. B. (Dept. Medicine, Univ. Texas Health Science Center, San Antonio, TX 78284) McGuire, W. L. *Cancer Res* 37(6): 1733-1738; 1977.

An investigation was made of the properties of progesterone receptor protein (PRP) demonstrated in 7,12-dimethylbenzanthracene-induced rat mammary tumors by the synthetic progestin, R5020. PRP binds hormone with high affinity (ie, with a Kd of about 1 nanomolarity) and migrates at 4S and 7S on sucrose density gradients. Ovariectomy plus adrenalectomy of the tumor-bearing rats resulted in regression of the mammary tumors and a fall in cytoplasmic PRP levels. The administration of progesterone alone failed to sustain tumor growth, but estradiol, alone or with progesterone, prevented tumor regression and loss of cytoplasmic PRP. (24 refs.)

77-4158 **Gonadotropin Receptors in Experimentally Induced Ovarian Tumors in Mice.** (Eng.) Kammerman, S. (Dept. Medicine, New York Univ. Medical Center, New York, NY 10016) Demopoulos, R. I.; Ross, J. *Cancer Res* 37(8/part 1): 2578-2582; 1977.

Since gonadotropic hormones are required for maintenance of ovarian tumors transplanted to gonadectomized mice, the receptors of human chorionic gonadotropin-luteinizing hormone were investigated in Swiss white mice. The number of receptors per cell was found to increase 17-fold with tumor induction. While varying size, duration and morphology of tumors did not affect receptor-binding affinity, the number of binding sites per cell increased with the degree of morphological luteinization of the tumor. (24 refs.)

77-4159 **Differences in Plasma Membrane Organization of Neuroblastoma Cells Grown in the Differentiated and Undifferentiated States.** (Eng.) Charalampous, F. C. (Dept. Biochemistry and Biophysics, Sch. Medicine, Univ. Pennsylvania, Philadelphia, PA 19174) *Arch Biochem Biophys* 181(1): 103-116; 1977.

Analysis was made of the enzymic complement and electrophoretic profile of plasma membrane (PM) fractions prepared by two methods from differentiated (monolayer-cultured) or undifferentiated (spinner-cultured) murine neuroblastoma (clone 2-A) cells. The methods are (1) a two-phase polymer and sucrose gradient system yielding "primary PM from monolayer-cultured cells was richer in $Na^+ + K^+$-activated ATPase, acetylcholinesterase, and choline acetyltransferase activities than that from spinner-cultured cells, but the polypeptide composition of these membranes was similar in both cell types. In contrast, internalized PM from monolayer-cultured cells differed significantly from that isolated from spinner-cultured cells in both enzymic content and polypeptide composition. Furthermore, the effects of dibutyryl cAMP and sodium butyrate on membrane properties were different in the two types of cells. The results support the conclusion that differentiation of the neuro-2A clone is accompanied by extensive changes in the organization and dynamics of the PM. (51 refs.)

77-4160 **Cell Membrane Architecture of Normal and Malignant Liver Cells in Culture (Meeting Abstract).** (Eng.) Borek, C. (Coll. Physicians and Surgeons, Columbia Univ., New York, NY 10032) Pain, C. *Proc Am Assoc Cancer Res* 18: 193; 1977. (no refs.)

77-4161 **BrdU-Induced Surface Changes in Liver Cells in Culture (Meeting Abstract).** (Eng.) Avdalovic, N. (Wistar Inst., Philadelphia, PA 19104) Diamond, L. *Proc Am Assoc Cancer Res* 18: 90; 1977. (no refs.)

77-4162 **BrdU-Giemsa-Technique for the Differentiation of Sister Chromatids in Somatic Cells of *Drosophila melanogaster*.** (Eng.) Wienberg, J. (Institut fur Genetik, Freie Universitat Berlin, Arnimallee 5-7, 1000 Berlin 33, W. Germany) *Mutat Res* 44(2): 283-286; 1977.

The mechanisms of sister chromatid exchange in *Drosophila melanogaster* were investigated by the bromodeoxyuridine-Giemsa staining technique. In spite of the rare occurrence of differential staining and the difficulty of scoring, the rate of exchanges in this species appears to be low. (26 refs.)

77-4163 **Experimental Heterotransplantation of Detroit-6/VA/Carcinomatous Cells into the Eyeball of Hypercholesterolemic Rabbits.** (Eng.) Schuller, L. (Medical Res. Center, Str. Lenin No. 31, Tirgu-Mures, Romania) Popa, D. P.; Kerekes, M.; Fodor, F.; Laszlo, I.; Ardeleanu, M.; Schuller, L. *Oncology* 33(506): 232-236; 1976.

Correlations between a cholesterol-rich diet and the growth of Detroit-6/VA/carcinomatous tumor transplanted into the eye were studied. A suspension of the tumor cells was injected into the anterior chamber and vitreous body of the left eyeball in 14 male adult white and grey rabbits. Nine of the animals were maintained on a high-cholesterol diet and five on a regular diet. The right eye in each of the animals served as a control. The mean wt of the left eyeball in the cholesterol-fed rabbits was 3.51 g, compared to a mean wt of 3.40 g for the right eyeball. In the animals maintained on a regular diet, the mean wt of the left eyeball was 3.47 g and that of the right eyeball was 3.42 g. Tumors reached mean sizes of 8.00 and 4.56 mm in the cholesterol-diet and normal-diet animals, respectively. Biochemical studies showed that the right eyeball contained more cholesterol and less protein than the left eyeball. The eyeballs of rabbits on a normal diet did not differ significantly in these parameters. It appeared that hypercholesterolemia of the eye had increased tumor growth. (14 refs.)

77-4164 **Serial Heterotransplantation of Human Breast Carcinoma in Newborn Rats.** (Eng.) Benjamin, I. (St. Louis Univ. Sch. Medicine, Dept. Pathology, 1402 S. Grand Blvd., St. Louis, MO 63104) Pinkerton, H. *Progr Clin Biol Res* 12: 71-74; 1977.

To date, a human breast carcinoma has been grown in 250 cortisonized newborn Sprague-Dawley rats. This model has the advantages of low cost, retention of much of the immunologic reactivity, and suitability for chemotherapeutic and metastatic studies. Histologically, the tumor is similar to the human ancestor. (1 ref.)

77-4165 **Inactivation of Transcription in Tumors During Serial Transplant (Meeting Abstract).** (Eng.) Shearer, R. W. (Issaquah Group for Health and Environmental Res., Issaquah, WA 98027) Dodge, A. H. *Proc Am Assoc Cancer Res* 18: 243; 1977. (no refs.)

77-4166 **Spin-Label Studies of Rat Peritoneal Mast Cells, Mouse Mastocytoma Cells and Compound 48/80 (Meeting Abstract).** (Eng.) Ortner, M. J. (Natl. Heart, Lung, and Blood Inst., NIH, Bethesda, MD 20014) Chignell, C. *Fed Proc* 36(3): 1042; 1977. (no refs.)

77-4167 **Proliferation of Myeloblasts and Promyelocytes from Untreated Patients with Acute Myelogenous Leukemia (AML) in Diffusion Chambers Implanted into Irradiated Rats: Characterization of Secondarily Derived Continuous Tissue Culture Lines (Meeting Ab-**

stract). (Eng.) Greenberger, J. S. (Peter Bent Brigham Hosp., Boston, MA 02115) Karpas, A.; Gans, P. J.; Moloney, W. C. *Proc Am Assoc Cancer Res* 18: 280; 1977. (no refs.)

77-4168 **Influence of Cell Size and Cycle Parameters on the Development of Artificial Pulmonary Metastases (Meeting Abstract).** (Eng.) Grdina, D. J. (Experimental Radiotherapy, M. D. Anderson Hosp. and Tumor Inst., Houston, TX 77030) Jones, S.; Chan, E.; Peters, L. J. *Proc Am Assoc Cancer Res* 18: 67; 1977. (no refs.)

77-4169 **Cell Renewal System of Tracheal Epithelium of Syrian Golden Hamster (Meeting Abstract).** (Eng.) Paradise, L. J. (Univ. South Florida Coll. Medicine, Tampa, FL 33620) Boren, H. G. *Proc Am Assoc Cancer Res* 18: 191; 1977. (no refs.)

77-4170 **Weight, Stroma to Gland Ratio, and Mitotic Activity of the Human Hyperplastic Prostate.** (Eng.) Pietila, J. (Inst. Biomedical Sciences, Univ. Tampere, Box 607, SF 33101 Tampere 10, Finland) Arvola, I.; Senius, K. E.; Tuohimaa, P. *Invest Urol* 15(1): 90-92; 1977.

An in vitro study of hyperplastic prostate growth using resected prostates from 12 patients indicated that growth is the result of both hyperplasia of the glandular epithelium and stromal hypertrophy. Therefore, an assay of the mitotic activity of biopsy specimens can be used to estimate the wt of the hyperplastic prostate. (15 refs.)

77-4171 **Patterns of Lobulo-Alveolar (LA) Mitotic Activity (MA) in the Rat Mammary Gland (MG) (Meeting Abstract).** (Eng.) Purnell, D. M. (Hershey Medical Center, Hershey, PA 17033) Stowers, D. J. *Proc Am Assoc Cancer Res* 18: 21; 1977. (1 ref.)

77-4172 **Establishment of Mouse Embryo Cells In Vitro. Relationship of DNA Synthesis, Senescence and Malignant Transformation.** (Eng.) Meek, R. L. (Div. Natural Sciences, Thimann Labs., Univ. California, Santa Cruz, CA 95064) Bowman, P. D.; Daniel, C. W. *Exp Cell Res* 107(2): 277-284; 1977.

The ability of BALB/c/CRL mouse embryo cells to proliferate decreases with increasing in vitro age. The ability of these monolayer cells to undergo DNA synthesis as a function of culture age was examined, and a progressive decline in the percentage of cells able to incorporate ^{3}H-thymidine was found. In this respect, they resembled normal human cells in culture. Instead of phasing out after a period of time, however, the mouse cultures were taken over by a continuously proliferating population of cells that displayed an elevated growth rate with a correspondingly large fraction of cells that incorporated ^{3}H-thymidine. Subsequent to this in vitro alteration, after the cultures had stabilized as a permanent cell line, the cells developed the ability to form tumors when tested in vivo. These results suggest that the acquisition of an indeterminate life span and a high growth rate in culture may be early events in a multistep process leading to malignancy. (41 refs.)

77-4173 **Binding of mRNA of Novikoff Hepatoma (NH), Normal Liver (NL) and Regenerating Rat Liver (RL) to cDNA-Cellulose (Meeting Abstract).** (Eng.) Hirsch, F. W. (Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX 77030) Rao, M. R.; Nall, K.; Raju, K. S.; Shoos, S. M.; Spohn, W. H.; Busch, H. *Proc Am Assoc Cancer Res* 18: 70; 1977. (no refs.)

77-4174 **Stimulation of DNA Synthesis by Human Placental Lactogen or Insulin in Organ Cultures of Benign Human Breast Tumors.** (Eng.) Welsch, C. W. (Dept. Anatomy, Michigan State Univ., East Lansing, MI 48824) McManus, M. J. *Cancer Res* 37(7): 2257-2261; 1977.

Twenty biopsy specimens of benign human breast tumors from 20 patients were processed into small slices and individually cultured for 2 days in medium 199. The medium was supplemented with bovine insulin (5.0 μg/ml), human placental lactogen (HPL) (10.0 μg/ml), or ovine prolactin (10.0 μg/ml). Four hours prior to termination, ^{3}H-thymidine was added to the culture medium to determine DNA synthesis. The addition of insulin to the culture medium consistently increased: (1) the mean incorporation of ^{3}H-thymidine into chemically extracted DNA ($p < 0.05$); (2) the mean number of ^{3}H-thymidine-radiolabeled epithelial cells ($p < 0.05$); and (3) the mean number of epithelial cells bearing mitotic figures. The addition of HPL increased the mean number of ^{3}H-thymidine-radiolabeled epithelial cells ($p < 0.05$) and the mean number of epithelial cells bearing mitotic figures ($p < 0.05$). ^{3}H-thymidine incorporation into chemically extracted DNA was also increased when HPL was added to the medium, although this increase did not quite achieve the 5% significance level. The addition of ovine prolactin to the culture medium did not have any significant effect on DNA synthesis. This study provides evidence that insulin and HPL are direct stimulants of DNA synthesis of the epithelium contained in benign human breast tumors. (33 refs.)

77-4175 **Inhibition of DNA Synthesis in Cultures of 3T3 Cells by Isolated Surface Membranes.** (Eng.) Whittenberger, B. (Dept. Biological Chemistry, Div. Biology and Biomedical Sciences, Washington Univ., St. Louis, MO 63110) Glaser, L. *Proc Natl Acad Sci USA* 74(6): 2251-2255; 1977.

When added to a sparse culture of 3T3 cells, a surface membrane-enriched fraction from 3T3 cells inhibited the rate of DNA synthesis in a time- and concentration-dependent manner. The membrane preparation had no effect on the DNA synthesis of simian virus 40-transformed 3T3 cells (SV3T3 cells). A similar membrane preparation from transformed cells had a lesser inhibitory effect on 3T3 cells and no effect on transformed cells. The inhibition by membranes was reversible. The data suggest that, when added to growing 3T3 cells, 3T3 surface membranes can mimic the effect of increasing cell density on DNA synthesis. Compared with 3T3 cells, SV3T3 cells are defective in their ability to receive and integrate growth regulatory signals. (23 refs.)

77-4176 **Role of Putrescine in DNA Synthesis and Mitosis of Mammalian Cells (Meeting Abstract).** (Eng.) Sunkara, P. S. (Dept. Developmental Therapeutics, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX 77030) Rao, P. N.; Nishioka, K. *Proc Am Assoc Cancer Res* 18: 84; 1977. (no refs.)

77-4177 **An Increased Requirement for Methionine By Transformed Rat Liver Epithelial Cells In Vitro (Meeting Abstract).** (Eng.) Wilson, M. J. (NIH, Bethesda, MD 20014) Poirier, L. A. *Proc Am Assoc Cancer Res* 18: 67; 1977. (no refs.)

77-4178 **Changes in the Structure of Nucleic Acids and Their Bonds with Metals in Leukemia Cells.** (Rus.) Bala, I. M. (Dept. Hosp. Therapy, Voronezh Medical Inst., Voronezh, USSR) *Probl Gematol Pereliv Krovi* 21(11): 21-24; 1976.

A spectrographic examination of the nucleic acids from leukemic WBC showed an increase in the amount of metals bound with the DNA molecule. Patients with chronic myeloid leukemia had an elevated concentration of copper (1.65 μg compared to 0.88 μg in controls), but patients with acute leukemia had an increased concentration of chrome (2.75 μg compared to 0.70 μg in controls). A significant increase of DNA-bound metals was also observed in the spleen, liver and blast cells from rats with transplanted Schvets leukemia. (11 refs.)

77-4179 **A Unique Property of Fetal Bovine Serum: High Levels of Protein-Glutathione Mixed Disulfides.** (Eng.) Bump, E. A. (Dept. Biochemistry and Biphysics, Oregon State Univ., Corvallis, OR 97331) Reed, D. J. *In Vitro* 13(2): 115-118; 1977.

The high levels of protein-glutathione mixed disulfides (3-7 μg glutathione as mixed disulfide/ml serum) in fetal bovine serum (FBS) were assessed. Three- and 5-mo FBS contained large amounts of mixed disulfide, but near-term FBS did not contain detectable amounts. The level of mixed disulfide could depend upon the period of gestation of the fetal calves used in preparing the serum. Sephadex G-200 fractionation of FBS showed the mixed disulfide content to be concentrated in a certain molecular wt range. Fetuin was a protein that was found only in FBS. Analysis of partially purified fetuin indicated that it contained a high level of protein-glutathione mixed disulfide, but fetuin-free fractions of FBS also contained high levels of mixed disulfides. Incubation of FBS with 1 mg/ml oxidized glutathione at 50 C for 24 hr, followed by filtration through Sephadex G-25 to remove oxidized glutathione, resulted in a serum that contained approx seven times more protein-glutathione mixed disulfide than untreated FBS. The reaction was slow at 37 C, and it was not completed in 24 hr. Calf, adult bovine, fetal horse, and swine sera do not contain detectable levels of this type of mixed disulfide in contrast to FBS. (16 refs.)

77-4180 **Glycopeptide Patterns of Mouse Mammary Glands and Tumors (Meeting Abstract).** (Eng.) Sheffield, J. B. (Inst. Medical Res., Camden, NJ 08103) Buck, C. A.; Warren, L. *Proc Am Assoc Cancer Res* 18: 189; 1977. (no refs.)

77-4181 **Novel Glycoproteins in Hepatocellular Carcinoma (Hepatoma) (Meeting Abstract).** (Eng.) Liu, C. (Mount Sinai Sch. Medicine, New York, NY 10029) Schreiber, C.; Schmied, R.; Waxman, S. *Proc Am Assoc Cancer Res* 18: 231; 1977. (1 ref.)

77-4182 Uptake and Turnover of ^{32}P-Phosphate and ^{14}C-Leucine in Chromosomal Proteins from Cultured Cells Derived from Normal (V-14B) and Neoplastic (T-19D) Mouse Mammary Tissue (Meeting Abstract). (Eng.) Lai, D. Y. (Cell and Molecular Biology, Medical Coll., Augusta, GA 30902) Howard, E. F.; Bustos, S. E. *Fed Proc* 36(3): 784; 1977. (no refs.)

77-4183 **Negatively Charged Phosphopeptides of Nucleolar Nonhistone Proteins from Novikoff Hepatoma Ascites Cells.** (Eng.) Mamrack, M. D. (Nuclear Protein Lab., Dept. Pharmacology, Baylor Coll. Medicine, Houston, Texas 77030) Olson, M. O.; Busch, H. *Biochem Biophys Res Commun* 76(1): 150-157; 1977.

Oligo- and poly-phosphopeptides were isolated from the nucleoli of Novikoff hepatoma ascites (NHA) cells, and the sites phosphorylated by endogenous kinases on these phosphopeptides were analyzed to determine if potential regulatory phosphoproteins exhibit common features in their sites of phosphorylation. NHA cells were transplanted into albino rats, and the nucleoli from these cells were isolated and analyzed after 6 days of incubation. Acid-soluble proteins from these nucleoli were separated via slab gel electrophoresis. The proteins from the bands were isolated, digested with trypsin, and the tryptic peptides separated by column chromatography. Band C23 was separated into tryptic phosphopeptide fractions A, B, and C, and Band B23 was separated into α and β fractions. Each of these fractions contained phosphoserine, had similar amino acid composition, was composed of at least 49 mole percent acidic residues and had molecular wts of 7-11,000. These data indicate that the C23 and B23 nonhistone proteins have similar phosphorylated regions of high negative charge. (21 refs.)

77-4184 **Relationship Between the Physicochemical Nature of Human Interferon, the Cell Induced, and the Inducing Agent.** (Eng.) Cesario, T. C. (Univ. California Irvine Medical Center, 101 City Drive South, Orange, CA 92668) Schryer, P. J.; Tilles, J. G. *Antimicrob Agents Chemother* 11(2): 291-298; 1977.

To determine the basis for the reported differences in interferons (IF's), five varieties of human IF were prepared: IF induced in muscle skin fibroblasts by complexed polyinosinic:-polycytidylic acid (IC) and Newcastle disease virus (NDV) and IF induced in WBC by IC, NDV, and phytohemagglutinin. The molecular wt, isoelectric point, and structural activity relationships were determined for each IF. The IF's derived from a given cell by different inducers were similar, but the IF's stimulated by the same inducer in different cells differed substantially in activity after electrofocusing, in heat stability, and in chemical stability. The pharmacologic implications of these findings for the use of IF in man are discussed. (21 refs.)

77-4185 **RNase Activity in Human Interferon Preparations.** (Eng.) Winchurch, R. A. (Baltimore Cancer Res. Center, NCI, Baltimore, MD 21211) Karpetsky, T. P.; Levy, C. C.; Cantell, K. *J Virol* 21(3): 1247-1248; 1977.

The level of RNase activity in human WBC interferon preparations was examined. Although sequential purification of interferon resulted in nearly a three-hundredfold increase in specific activity. RNase-specific activity remained more or less constant. The implications of this finding for analyses of the mode of action of interferon are discussed. for analyses of the mode of action of interferon are discussed. (10 refs.)

77-4186 **Isolation of a Unique DNA Polymerase from Human Milk (Meeting Abstract).** (Eng.) Kantor, J. A. (Dept. Biochemistry, Georgetown Univ., Washington, DC 20007) Lee, Y. H.; Chirikjian, J.; Feller, W. F. *Proc Am Assoc Cancer Res* 18: 67; 1977. (no refs.)

77-4187 **Nuclear Phosphoproteins and Phosphoprotein Kinases in Human Hepatoma (Meeting Abstract).** (Eng.) Belanger, L. (Dept. Biochemistry, Sch. Medicine, Vanderbilt Univ., Nashville, TN 37232) Chiu, J. F. *Proc Am Assoc Cancer Res* 18: 203; 1977. (no refs.)

77-4188 **Nucleolar Associated Phosphoprotein Kinases of Normal Rat Liver and Novikoff Hepatoma Ascites Cells (NHAC) (Meeting Abstract).** (Eng.) Olson, M. O. (Nuclear Protein Lab., Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX 77030) Hawkins, T. C. *Proc Am Assoc Cancer Res* 18: 83; 1977. (no refs.)

77-4189 **Distribution of the Polyamines and Their Biosynthetic Enzymes Between Nucleus and Cytoplasm in Rat Brain Tumor Cells (Meeting Abstract).** (Eng.) Heby, O. (Dept. Zoophysiology, Univ. Lund, Helgonavagen 3, S-223 62 Lund, Sweden) *Proc Am Assoc Cancer Res* 18: 79; 1977. (1 ref.)

77-4190 **Ultrastructural Localization of Enzymes of the Membranes and RNP-Structures of the Nuclei of Normal and Neoplastic Cells.** (Eng.) Raikhlin, N. T. (Lab. Histochemistry and Electron Microscopy, Dept. Pathological Anatomy and Human Tumors, Oncological Res. Center, Acad. Medical Sciences USSR, Moscow 115478, USSR) Bukhvalov, I. B.; Unger, E. *Folia Histochem Cytochem (Krakow)* 14(4): 217-221; 1976.

The ultrastructural localization of β-glycerophosphatase, glucose-6-phosphatase, ATPase and NADPH dehyrogenase was investigated in isolated rat and mouse liver nuclei and in nuclei isolated from the rat hepatomas 46, 22a, 27, and the Zajdela hepatoma. β-Glycerophosphate was not detectable and glucose-6-phosphatase was markedly reduced in hepatoma 27 nuclei. Nuclei from hepatomas 22a, 27, and 46 exhibited reduced magnesium-dependent ATPase activity; however, the activity of this enzyme in the nuclear membranes was markedly decreased in hepatomas 22a and 46 and enhanced in hepatoma 27. The activity of NADPH dehydrogenase in the nuclear membrane of the Zajdela hepatoma was 50% lower than in normal hepatocyte nuclei. Changes in the activity of the oxidative and dephosphorylating enzymes in the nuclei of neoplastic cells are not necessarily linked to cell transformation; they may reflect cell properties such as adaptation, degree of differentiation, or cell cycle phase. (19 refs.)

77-4191 **Enhancement of the Tumor Potential of Preneoplastic Mammary Cells by Enzymatic Dissociation (Meeting Abstract).** (Eng.) Medina, D. (Dept. Cell Biology, Baylor Coll. Medicine, Houston, TX 77030) Shepherd, F. *Proc Am Assoc Cancer Res* 18: 84; 1977. (no refs.)

77-4192 **Enzymes of Folate Metabolism in Experimental Tumor Systems (Meeting Abstract).** (Eng.) Albrecht, A. M. (Sloan-Kettering Inst., New York, NY 10021) Rogers, S. R.; Zorzo, S.; Boldizsar, E.; Hutchison, D. J. *Proc Am Assoc Cancer Res* 18: 227; 1977. (no refs.)

77-4193 **Ganglioside Biosynthesis. Characterization of CMP-N-Acetylneuraminic Acid: Lactosylceramide Sialyltransferase in Golgi Apparatus from Rat Liver.** (Eng.) Richardson, C. L. (Dept. Biological Sciences, Purdue Univ., West Lafayette, IN 47907) Keenan, T. W.; Moore, D. J. *Biochem Biophys Acta* 488(1): 88-96; 1977.

The sialyltransferase of rat liver Golgi apparatus that is involved in GM_3 synthesis is characterized. This enzyme transfers sialic acid from cytidine 5′-monophosphate-sialic acid to lactosylceramide. Evidence is given that the activity of this enzyme may be sensitive to end-product inhibition and that the vitamin A status may influence the levels of this activity in the rat liver. (49 refs.)

77-4194 **Terminal Transferase: Enzyme Marker for a Specific Prothymocyte Cell Population (Meeting Abstract).** (Eng.) Pazmino, N. H. (Basic Res. Program, NCI Frederick Cancer Res. Center, Frederick, MD 21701) McEwan, R. N.; Ihle, J. N. *Proc Am Assoc Cancer Res* 18: 81; 1977. (no refs.)

77-4195 **Biochemical Investigations of Separated Epithelium and Stroma from Benign Hyperplastic Prostatic Tissue.** (Eng.) Cowan, R. A. (Univ. Dept. Steroid Biochemistry, Royal Infirmary, Glasgow, G4 OSF, Scotland) Cowan, S. K.; Grant, J. K.; Elder, H. Y. *J Endocrinol* 74(1): 111-120; 1977.

Studies of benign hyperplastic prostate glands indicated that dehydroepiandrosterone sulfate sulfatase activity is localized primarily in the epithelium, but testosterone α-reductase activity is localized primarily in the stroma. These enzymes may regulate the intracellular concentration of 5α-dihydrotestosterone in androgen-responsive cells. (32 refs.)

77-4196 **Characteristics of the Cyclic Nucleotide Phosphodiesterases of Normal and Leukemic Lymphocytes.** (Eng.) Hait, W. N. (Dept. Pharmacology, Medical Coll. Pennsylvania, Philadelphia, PA 19129) Weiss, B. *Biochim Biophys Acta* 497(1): 86-100; 1977.

The properties of drugs and their effects on cyclic nucleotide phosphodiesterases (PDE's) of normal (from DBA, CDF, and Swiss Webster mice) and L5178Y and L1210 leukemic lymphocytes (LL) were studied. The LL had a 5-10 times greater activity of both cyclic AMP and cyclic guanosine monophosphate (GMP) PDE than did normal lymphocytes. A Ca-dependent activator of PDE was present in both normal and LL. However, this activator failed to increase the PDE activity of LL. Also, the PDE activity of LL was not inhibited by the Ca chelator ethyleneglycol-bis-(β-aminoethylether)-N,N′-tetraacetic acid, suggesting that the enzyme was not already maximally activated. The PDE's from normal and LL had similar pH optima, similar stabilities to freezing and thawing, and similar sensitivities to inhibition by chlorpromazine, papaverine, and isobutylmethylxanthine. There were differences in the subcellular distribution and heat stability of the PDE's--the PDE of LL was much more heat resistant than that of normal lymphocytes. There is also a greater quantity of PDE in LL. Concentrations of chlorpromazine that inhibited cerebral PDE by 70% failed to inhibit the PDE of normal or LL, but papaverine, a drug that is an effective inhibitor of nonactivatable PDE isoenzymes, inhibited the PDE of lymphocytes and cerebrum similarly. The differential drug-induced inhibition of PDE activity of brain and lymphocytes suggests that normal and LL may have a pattern of PDE isoenzymes that is different from other tissues, such as brain. Since an optimal concentration of cyclic nucleotides is required for normal cell growth, selective reduction of PDE activity in LL might inhibit their growth without adversely affecting the metabolism of other tissues. (56 refs.)

77-4197 **Enzymatic Aspects of Intestinal Epithelium.** (Eng.) Balis, M. E. (Lab. Cell Metabolism, Memorial Sloan-Kettering Cancer Center, New York, NY 10021) *Semin Oncol* 3(4): 337-340; 1977.

The enzymatic aspects of the intestinal epithelium are discussed. Thymidine kinase (TdRK) catalyzes the conversion of thymidine to thymidylic acid and plays a regulatory role in cell division. This enzyme is active only in crypt cells in normal intestine, but can be activated in the flat mucosal cells by the enzyme phospholipase C. This suggested that there might be specific forms of enzymes in the intestinal mucosa. To evaluate this premise, thymidine kinase was purified from human cadaver intestines, and antibodies were raised to it in rabbits. The antibody was able to neutralize the activity of the TdRK from normal and malignant mucosa to a greater extent than the TdRK from tumor or placenta. This suggested that fundamental differences exist between the enzymes from different sources. Phosphoribosyltransferases also revealed variants in different parts of the villus. Another intestinal enzyme studied was ornithine decarboxylase (ODC). In the gastrointestinal tract, the ODC values ranged from 4 in the colon to more than 1,000 in the ileum. The two parts of gastrointestinal tract with the highest incidence of cancer in man demonstrated the lowest value of ODC. To determine if DNA excision and repair mechanisms differ in the colon from those in the small bowel, the DNA of rats was labeled with tritiated thymidine. The rats were killed and the mucosa of the colon was separated into surface and crypt areas. The cells were then exposed to carcinogenic and noncarcinogenic materials, which form covalently bound adducts to DNA. Repair of DNA damage was much more rapid in the crypt cells following the administration of a carcinogenic compound. The results of these studies indicate that changes in the nondividing cells have a relationship to cancer of the bowel. Enzyme specificities of the tumors suggest that they may be derived from surface cells. (13 refs.)

77-4198 **Effects of Sugars on Melanogenesis in Cultured Melanoma Cells.** (Eng.) Nakayasu, M. (Biochemistry Div., Natl. Cancer Center Res. Inst., Tokyo 104, Japan) Saeki, H.; Tohda, H.; Oikawa, A. *J Cell Physiol* 92(1): 49-55; 1977.

A permanent cell line (C_2M) of mouse melanoma B16 was highly melanized in a modified Eagle's minimum essential medium (MEM) supplemented with 10% calf serum and containing 1 mM galactose and 10 mM pyruvate instead of 5.5 mM glucose. The activity of tyrosinase, the key enzyme for the melanogenesis of living cells, was consistently 27 times higher in cells cultured in the modified medium than in cells cultured in normal MEM. This high level of tyrosinase activity was maintained in the stationary phase, in contrast to the activity of the cells in normal medium, which decreased sharply in this phase. Tyrosinase activity is apparently suppressed by the presence of glucose rather than stimulated by galactose. The modified medium should be useful for obtaining a high level of tyrosinase activity in living cells in culture and in cell-free extracts. (18 refs.)

77-4199 **Modulation of Adenylate Cyclase Activity of Fibroblasts by Free Fatty Acids and Phospholipids.** (Eng.) Anderson, W. B. (Lab. Molecular Biology, NCI, NIH, Bethesda, MD 20014) Jaworski, C. J. *Arch Biochem Biophys* 180(2): 374-383; 1977.

The effect of certain lipids on adenylate cyclase activity [ATP pyrophosphate-lyase (cyclizing), EC 4.6.1.1] was investigated in cultured fibroblasts. The unsaturated fatty acids and lysolecithin acted as potent inhibitors of fibroblast adenylate cyclase activity. Increasing the degree of unsaturation increased the extent of inhibition at a given fatty acid concentration. The inhibitory effect of the unsaturated fatty acids or lysolecithin was not selective for a specific function of the adenylate cyclase system, as basal, and hormone- or fluoride-stimulated cyclase activities were inhibited to the same extent. The fatty acid-inactivated state of fibroblast adenylate cyclase was not readily reversed. The addition of unsaturated fatty acids or lysolecithin over a narrow concentration range (0.1-0.2mM) led to partial restoration of guanosine triphosphate activation of adenylate cyclase activity of Moloney sarcoma virus-transformed normal rat kidney (MNRK) fibroblasts. However, hormonal responsiveness to L-epinephrine or prostaglandin E was not restored to the MNRK enzyme with fatty acid or lysolecithin treatment. (32 refs.)

77-4200 **Fatty Acid Composition and Unsaturation of Intracellular Membrane Phospholipids from Rat Liver and Hepatoma 27.** (Rus.) Einisman, L. I. (Shemyakin Inst. Bioorganic Chemistry, Acad. Sciences USSR, Moscow, USSR) Gorkova, N. P.; Diatlovitskaia, E. V. *Biokhimiia* 42(2): 320-329; 1977.

The fatty acid composition of mitochondrial and microsomal phospholipids was studied in rat liver and hepatoma 27 cells, and the unsaturation of the lipid bilayer of the intracellular membranes was calculated. The unsaturation of the phospholipids of the hepatoma mitochondria and microsomes was found to be much lower than that of the corresponding rat liver membranes. The lipid bilayer of the rat liver and hepatoma plasma membranes was shown to be more saturated than that of the intracellular membranes. (23 refs.)

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CARCINOGENESIS ABSTRACTS

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CARCINOGENESIS ABSTRACTS

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CARCINOGENESIS ABSTRACTS

VOLUME 15, ISSUE 8

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CARCINOGENESIS ABSTRACTS makes available abstracts, annotations or citations of significant carcinogenesis articles collected from the current major biomedical sources of world literature. This service is provided by the National Cancer Institute through a contract with The Franklin Institute Research Laboratories for preparation of the publication, under Contract No. NOI-CP-75885 with the National Cancer Institute, U.S. Department of Health, Education and Welfare. Published and distributed by The Franklin Institute Press^{SM}.

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ABBREVIATIONS

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LANGUAGE of the article is indicated in parentheses after the title and is represented by a three-letter code. The source for these codes is *MARC Manuals Used by the Library of Congress,* pages 183-187.

ABBREVIATIONS used in abstracts:

A	angstrom(s)
ACTH	adrenocorticotropic hormone
ADP	adenosine diphosphate
AMP	adenosine monophosphate
ATP	adenosine triphosphate
approx	approximately
av	average
BCG	bacillus Calmette-Guerin
bid	twice daily
C	degree(s) centigrade
cal	calorie(s)
kcal	kilocalorie(s)
cc	cubic centimeter(s)
Ci	curie(s)
mCi	millicurie(s)
μCi	microcurie(s)
cm	centimeter(s)
CNS	central nervous system
cpm	counts per minute
DNA	deoxyribonucleic acid
ED_{50}	median effective dose
EDTA	ethylenediamine tetraacetic acid
g	gram(s)
kg	kilogram(s)
mg	milligram(s)
μg	microgram(s)
Hb	hemoglobin
hr	hour(s)
ia	intra-arterial
id	intradermal
IgA	Immunoglobulin A
IgB	Immunoglobulin B
IgG	Immunoglobulin G
IgM	Immunoglobulin M
ILS	increased life span
im	intramuscular
ip	intraperitoneal
IU	International Unit(s)
iv	intravenous
Km	Michaelis constant
LD	lethal dose
LD_{50}	median lethal dose
M	molar
μM	micromolar
mOsm	milliosmolar
max	maximum
mEq	milliequivalent(s)
min	minute(s)
ml	milliliter(s)
μl	microliter(s)
mm	millimeter(s)
mo	month(s)
mol wt	molecular weight
N	normal concentration
NAD	nicotinamide adenine dinucleotide
NADH	reduced nicotinamide adenine dinucleotide
NADP	nicotinamide adenine dinucleotidephosphate
NADPH	reduced nicotinamide adenine dinucleotidephosphate
NCI	National Cancer Institute
NIH	National Institutes of Health
PAS	periodic acid-Schiff
po	orally
ppb	parts per billion
ppm	parts per million
qid	four times daily
qod	every other day
QO_2	oxygen quotient
R	roentgen
RBC	red blood cells (erythrocytes)
RNA	ribonucleic acid
rpm	revolutions per minute
sc	subcutaneous
sec	second(s)
SGOT	serum glutamic-oxaloacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
soln	solution
TCD	tissue culture dose
TCD_{50}	median tissue culture dose
tid	three times daily
UV	ultraviolet
WBC	white blood cells (leukocytes)
wk	week(s)
wt	weight
X	times
yr	year(s)

77-4201 **Introduction to Experimental Geooncology.** (Fre.) Tran Ba Loc, P. (Laboratoire de Zoologie et Cancerologie Experimentale, Faculte de Medicine et de Pharmacie, 4, Place Saint-Jacques, 25000 Besancon, France) *Med Biol Environ* 4(1): 60-63; 1976.

In this brief review of environmental factors in oncogenesis, it is suggested that data obtained in the study of geooncology can be supported by animal experiments. The role of air and water pollutants, drugs, food, and viruses is mentioned. (14 refs.)

77-4202 **The Concept of Geooncology.** (Fre.) Peeters, E. G. (European Inst. Ecology and Oncology, Brussels, Belgium) *Med Biol Environ* 4(1): 10-25; 1976.

Geooncology is a discipline concerned with (1) ecology, pedology, climatology, social environment, and life style and (2) etiopathology and clinical evolution of cancer. Various factors involved in the incidence of cancer are discussed, including heat, soil composition, exposure to sunlight, organisms such as Schistosoma, and unusual local customs. Two tables give cancer mortality data for the time periods 1900-02, 1928-30, and 1958-60 for 22 countries. A third table gives data on cancer mortality from cancers of the stomach, respiratory system, breast, uterus, prostate, and leukemias in these countries for 1950-52 and 1958-60. Cancer frequency according to site in different regions of the world is summarized, and unusually high incidences in particular countries are listed. Known or theoretical etiological factors in hepatomas and cancers of the colon, rectum, penis, and cervix are reviewed. Information on geooncology should be integrated into international programs such as those undertaken by the United Nations. (26 refs.)

77-4203 **Closing Words by Dr. Emile-Gaston Peeters, International Secretary General of INEC.** (Fre.) Peeters, E. G. (European Inst. Ecology and Oncology, Brussels, Belgium) *Med Biol Environ* 4(1): 78-81; 1976.

The new concept of geooncology developed at the International Symposium of the European Institute of Ecology and Oncology (INEC) on Cancer and the Environment, Brussels, November, 1973, is discussed. Geooncology includes, on the one hand, data on ecology, pedology, climatology, social environment, and life style and, on the other hand, the etiology, clinical evolution, distribution, and frequency of different types of cancer. Integration of geooncological data into programs undertaken by the World Health Organization and other specialized programs of the United Nations is emphasized. (no refs.)

77-4204 **Geographic Oncology and Epidemiology. Environmental Oncology of Physical and Chemical Carcinogens in Global Oncology.** (Fre.) Mosinger, M. (Institut de Synthese et Prospective de Recherche biomedicale et biophysique et d'expertise scientifique, Marseille, France) *Med Biol Environ* 4(1): 4-5; 1976.

Epidemiological research on cancer can produce valuable data, such as the studies on Burkitt's lymphoma, when the methodology is appropriate and the geographical region is chosen carefully. In most cancers, exogenous and endogenous factors interact in a complex manner, and a system is proposed for defining some of these factors in epidemiological studies. (1) For any geographic area, a profile of the environment should be obtained by measuring the physical, chemical, macrobiotic, microbiological, viral, and psychosociological parameters of the area. (2) In addition, data should be gathered on the inhabitants of the geographical area, including heredity, clinical family history, histology, physiology, and psychology and the bacteria and viruses that they might carry. Such a profile would be called a biogram. Statistical analysis of these data could lead to important fundamental information on human carcinogenesis. (no refs.)

77-4205 **The Geographical Pathology of Mesothelial Tumors.** (Eng.) Newhouse, M. L. (TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, Keppel St. at Gower St., London, WC1E 7HT, England) *J Occup Med* 19(7): 480-482; 1977.

Current information is reviewed concerning the occurrence of mesotheliomas in asbestos mining areas in South Africa, Canada, the United Kingdom, and Europe. The length and diameter of the fibers influence their ability to penetrate the lung, thus accounting for the preponderance of tumors in areas where crocidolite is mined. Amosite and chrysotile asbestos, both slightly longer and less penetrating fibers, appear to be somewhat less pathogenic than crocidolite. A review of data from European areas shows a concentration of cases near ports and shipyards and in industrial areas where mixed exposures are the rule. Mesothelial tumors reported throughout Europe are mapped. (18 refs.)

77-4206 **The Dangers of Asbestos.** (Eng.) Anonymous (No affiliation given) *JAMA* 238(9): 980; 1977.

British scientists who studied the toxic effects of asbestos found that there was a 1% chance that an asbestos-related disease would develop in a person exposed to approx 2 fibers per cubic centimeter of ambient air for 50 yr and that exposure for 25 yr produced a mortality 30% higher than that in the general population. (no refs.)

77-4207 **Pneumoconioses.** (Eng.) Hanson, R. R. (Dept. Internal Medicine, Iowa Methodist Medical Center, 1200 Pleasant St., Des Moines, IA 50308) Kasik, J. E. *Heart Lung* 6(4): 646-652; 1977.

The etiologic role of asbestos in human carcinoma is reviewed. Attention is also focused on other pneumoconioses and on berylliosis, which is manifest in lung granulomas. (33 refs.)

77-4208 **Relationships of Quantum Mechanical Calculations, Relative Mutagenicity of Benzo(a)anthracene Diol Epoxides, and "Bay Region" Concept of Aromatic Hydrocarbon Carcinogenicity.** (Eng.) Lehr, R. E. (Dept. Chemistry, Univ. Oklahoma, 620 Parrington Oval, Norman, OK 73019) Jerina, D. M. *J Toxicol Environ Health* 2(6): 1259-1265; 1977.

The use of quantum mechanical calculations to predict the reactivity of diol epoxides of polycyclic aromatic hydrocarbons is discussed. These calculations predict that diol epoxides in which the oxirane ring forms part of a "bay region" of a tetrahydrobenzo ring should be the most reactive for a given aromatic hydrocarbon. Experiments were performed to determine the mutagenicity of various dihydrodiols and diol epoxides of benzo(a)anthracene (BA). The ability to activate BA-3,4-dihydrodiol to species more mutagenic in the Ames test than those from other BA dihydrodiols and the greater mutagenicity of the diastereoisomeric 3,4-diol-1,2-epoxides of 1,2,3,4-tetrahydro-BA than the other diol epoxides of BA agreed with the predictions of the quantum mechanical calculations. (22 refs.)

77-4209 **Study Links Saccharin to Cancer in Humans.** (Eng.) Anonymous (No affiliation given) *FDA Consum* 11(6): 3; 1977.

Various legal and scientific facts that form the basis for the proposed FDA ban on saccharin are reviewed. A Canadian study showed that men who consume saccharin are at a greater risk of developing bladder cancer. (no refs.)

77-4210 **Saccharin and Cancer (Letter to Editor).** (Eng.) Homburger, F. (Bio-Res. Inst., Inc., Cambridge, MA 02141) *N Engl J Med* 297(10): 560-561; 1977.

The validity of the Canadian study on saccharin is questioned because bladder lesions in rats may be caused by *Trichosomoides crassicauda*, as well as by natural carcinogens in food or hormonal imbalance. Further studies should be performed on other species (eg, hamsters) that are susceptible to bladder carcinogens known to affect humans (eg, β-napthylamine). (2 refs.)

77-4211 **Validity of Animal Testing (Letter to Editor).** (Eng.) Cohn, W. E. (Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830) *Chem Eng News* 55(35): 5; 1977.

The validity of animal tests that prove the carcinogenicity of saccharin in man is challenged. Animal tests apparently do not take into account detoxification mechanisms, repair mechanisms, and differences in metabolism between animals and man. (no refs.)

77-4212 **Dietary Fat Affects Tumor Growth in Rats.** (Eng.) Anonymous (No affiliation given) *Chem Eng News* 55(36): 22; 1977.

Groups of rats were given 2-acetylaminofluorene (AAF) ip and in their diet after 8 mo of receiving diets containing either corn oil or tallow. Rats fed corn oil diets excreted more urinary N-hydroxyacetylaminofluorene, a metabolite of AAF and also a hepatocarcinogen. The livers of animals fed corn oil and AAF were more necrotic and more severely damaged by neoplasms. (no refs.)

77-4213 **N-Nitroso Compounds: Their Chemical and In Vivo Formation and Possible Importance as Environmental Carcinogens.** (Eng.) Mirvish, S. S. (Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, Omaha, NB 68105) *J Toxicol Environ Health* 2(6): 1267-1277; 1977.

A review is presented of the occurrence of N-nitroso compounds and of their possible role in human carcinogenesis.

The topics covered include the occurrence of N-nitroso compounds; the chemistry and kinetics of their formation; the in vivo production of N-nitroso compounds; the evaluation of hazards due to specific nitrosatable compounds; the carcinogenicity of new N-nitrosamides; the possible induction of cancer in humans by N-nitroso compounds; esophageal cancer in humans and tritiated thymidine incorporation studies with the rat esophagus; the hypothesis that gastric cancer in humans is due to N-nitrosamides. (51 refs.)

77-4214 **Metabolic Activation of Hepatotoxins and Carcinogens: Induction by Alcohol and Drugs.** (Fre.) Hetu, C. (Departement de medecine, Hopital Saint-Luc, 1058, St-Denis, Montreal, Quebec, H2X 3J4, Canada) *Union Med Can* 106(5): 631-635; 1977.

The carcinogenic effects of certain compounds may occur as a result of their transformation by the cytochrome P-450-dependent hepatic microsomal enzyme system into activated metabolites more toxic than their precursors. These metabolites covalently bind to cellular proteins and, sometimes, to nucleic acids. Alcohol, drugs, and other liposoluble substances, which act as inducers of the cytochrome P-450 system, can result in higher rate of formation of the activated metabolites. The ethanol-induced cytochrome P-450 system is particularly active in the biotransformation of aniline, an aromatic amine from a class of compounds known to be hepatotoxic or carcinogenic. It is hypothesized that alcohol can increase the susceptibility of an individual to the hepatotoxic or carcinogenic actions of many compounds that are industrial environmental pollutants. A scheme is given for the theoretical metabolic activation of carcinogens in relation to biotransformation pathways of exogenous substances. (24 refs.)

77-4215 **Mutational Approaches to the Study of Carcinogenesis.** (Eng.) Chu, E. H. (Dept. Human Genetics, Univ. Michigan Medical Sch., Ann Arbor, MI 48109) Trosko, J. E.; Chang, C. C. *J Toxicol Environ Health* 2(6): 1317-1334; 1977.

The available experimental evidence concerning carcinogenesis was reexamined to determine whether it supports or contradicts the somatic mutation theory of cancer. In addition, based on recent findings a new integrative theory of carcinogenesis is proposed that encompasses both genetic and epigenetic mechanisms. The concept that neoplasms arise from mutations in somatic cells was originally introduced to account for the unlimited variety of tumor types and the fact that, on cell division, daughter cells maintain their neoplastic properties. The predictions of the somatic mutation theory, various experimental approaches to test the theory, and observations that are consistent or inconsistent with the expectations are listed. This is followed by a discussion of the two-stage process of carcinogenesis and mutagenesis. If it is assumed that (1) in vitro neoplastic transformation can reflect the process in vivo, (2) the two-stage process of carcinogenesis (initiation and promotion) involves a mutagenic step, and (3) DNA repair is involved in initiation, then the role of tumor modifiers, such as phorbol esters and caffeine, might give insight into the molecular basis for in vitro and in vivo neoplastic transformation. Mutagenesis is considered responsible for initiation and an epigenetic mechanism responsible for promotion. Carcinogenic agents can induce a stable transformation of a cell by either mutation or epigenetic alterations in gene expression. Based on this conclusion, a new integrative theory of carcinogenesis is proposed that encompasses the tenets of four main theories: (1) the mutation and epigenetic basis for carcinogenesis, (2) the two-stage theory, (3) Comings' general theory, and (4) the somatic deletion mutation theory. (91 refs.)

77-4216 **Genetic Aspects of Toxicity During Development.** (Eng.) Nebert, D. W. (Developmental Pharmacology Branch, Natl. Inst. Child Health and Human Development, NIH, Bethesda, MD 20014) Thorgeirsson, S. S.; Lambert, G. H. *Environ Health Perspect* 18: 35-45; 1977.

Teratogenicity in C57BL/6N mice is associated with the administration of 3-methylcholanthrene and 7,12-dimethylbenz(a)anthracene to the pregnant mother. These effects are not observed in AKR/N mice. The hepatotoxicity of acetaminiphen was found to be associated with the *Ah* locus and glutathione depletion in the liver. (55 refs.)

77-4217 **Genetic and Cytogenetical Effects of Formaldehyde and Related Compounds.** (Eng.) Auerbach, C. (Inst. Animal Genetics, Univ. Edinburgh, West Mains Road, Edinburgh, EH9 3JN, Scotland) Moutschen-Dahmen, M.; Moutschen, J. *Mutat Res* 39(3/4): 317-361; 1977.

The chemical properties and toxic genetic and cytologic effects of formaldehyde, other aldehydes, and precursor molecules are reviewed. Human exposure to these compounds could result from their use in agriculture, from air pollution, cigarette smoke, disinfectants, medicinal drugs, and foods exposed to ionizing radiation. (189 refs.)

77-4218 **Aryl Hydrocarbon Hydroxylase Induction (*Ah* Locus) as a Possible Genetic Marker for Cancer.** (Eng.) Nebert, D. W. (Developmental Pharmacology Branch, Natl. Inst. Child Health and Human Development, NIH, Bethesda, MD 20014) Atlas, S. A. *Prog Cancer Res Ther* 3: 301-319; 1977.

A current view is provided of the enzyme systems that metabolize most environmental carcinogens, the genetic regulation of these enzymes in the mouse, the association of the mouse *Ah* locus with increased susceptibility to chemical carcinogenesis, and attempts at defining the *Ah* locus in man. In general, environmental contaminants are metabolized by a group of membrane-bound enzymes known as the cytochrome P-450-mediated monooxygenases. Possible pathways during the metabolism of benzo(a)pyrene (BP) are illustrated, and factors influencing the steady-state level of the proximal chemical carcinogen in the cell are presented. The current concept of AHH activity using BP as a substrate is illustrated. The magnitude of AHH and cytochrome P_1-450 induction by polycyclic hydrocarbons appears to be regulated genetically in most tissues of the mouse. Differences in metabolites produced by different forms of cytochrome P-450 are also reviewed. In the search for the *Ah* locus in man, two 1973 reports that gave initial hope to clinical geneticists and oncologists are summarized. It is possible that the monooxygenation of BP is under relatively simple genetic control in man and that this singular response (ie, AHH induction in cultured lymphocytes) can be correlated with increased risk of bronchogenic carcinoma. An association with the *Ah* locus has been demonstrated for 3-methylcholanthrene (MC)- and BP-initiated sarcomas and MC-initiated lung cancer in two strains of mice. In one study in humans, intratwin variance between identical twins was statistically significantly less than that between fraternal twins with regard to the fold induction of AHH activity in cultured mitogen-activated lymphocytes. (77 refs.)

77-4219 **Oestrogen Treatment and Endometrial Carcinoma (Letter to Editor).** (Eng.) Feinstein, A. R. (Sch. Medicine, Yale Univ., New Haven, CT) Horwitz, R. I. *Br Med J* 2(6089): 766-767; 1977.

A recent article failed to cite two case control studies showing no association between estrogen use and endometrial cancer. Moreover, estrogens given to women with undetected endometrial cancer will be mistakenly associated with the etiology of the cancer when it is diagnosed later. In women with asymptomatic cancer, estrogens may provoke bleeding which will lead to diagnosis. (2 refs.)

77-4220 **Thyroid Hormone and Breast Cancer (3 Letters to Editor).** (Eng.) Venezian, E. C. (Cambridge, MA) MacCornack, F. A.; Taylor, W. F.; Hayles, A. B. *JAMA* 238(11): 1147-1148; 1977.

Retrospective studies of breast cancer incidence among women receiving thyroid hormone therapy can yield valid results if data are adjusted for relevant variables such as age. Further analysis of data on the breast cancer-thyroid supplement association suggests that younger (premenopausal) women are actually at higher risk for increased breast cancer incidence with thyroid hormone usage. Although the percentage of women with breast cancer increases significantly with age, it is the younger women who are affected by use of thyroid medication in proportion to duration of treatment. (2 refs.)

77-4221 **Injectable Contraceptives.** (Eng.) Anonymous (No affiliation given) *Lancet* 2(8035): 441; 1977.

Medroxyprogesterone acetate is a long acting injectable contraceptive that causes breast nodules in beagles; it may predispose a user to cervical cancer, but the lack of a control group hampers evaluation of risk to humans. Norethisterone enanthate, a similar product, causes breast nodules in rats and mice. These preparations are banned in the United States but are used elsewhere in the world. (6 refs.)

77-4222 **Does Rauwolfia Cause Breast Cancer?** (Eng.) Anonymous (No affiliation given) *Br Med J* 2(6089): 757; 1977.

Although the association between rauwolfia and breast cancer is not conclusively established, the fact that there may be an association is sufficient to recommend use of another agent to control hypertension. (6 refs.)

77-4223 **Toxicology in Cancer Research. II. Carcinogenic Drugs.** (Ger.) Schmahl, D. (Institut fur Toxicologie und Chemotherapie Deutsches Krebsforschungszentrum, 6900 Heidelberg, Im Neuenheimer Feld 280, W. Germany) *Dtsch Med Wochenschr* 102(29): 1047-1050; 1977.

A review of toxicology in cancer research is given, with emphasis on detoxication of endogenous carcinogens, their mode of action, dose-response relations, and cancer chemotherapy. Carcinogenic drugs (primarily alkylating agents) that may cause iatrogenic carcinomas are listed. Numerous endogenous substances originating in the stomach are also implicated as carcinogens (nitrosamines). Observations indicate that detoxication, even in the case of endogenous carcinogens, is still possible. For example, the formation of nitrosamines from nitrite and amines can be prevented by ascorbic acid. Chemical carcinogens in the genetic material of the cell will eventually damage the nucleic acids. The action of most carcinogens is irreversible. The smallest doses of these agents are additive, resulting in malignant transformation of the normal cell. Most chemotherapeutic drugs are associated with severely toxic side effects. Because of this and because of the high doses necessary for antitumor action, they are frequently rejected. (20 refs.)

77-4224 **Alkylating Agent Linked to Occurrence of Leukemias as Second Cancers.** (Eng.) McBride, G. (No affiliation given) *JAMA* 237(25): 2697-2699; 1977.

Treatment with alkylating agents (including melphalan, chlorambucil, cyclophosphamide, thio-tepa, and uracil mustard) appears to increase the incidence of acute leukemia. Investigators call for a new, hard look at the use of these agents, particularly in the adjuvant chemotherapy of breast cancer, but also in the treatment of ovarian and other cancers. (1 ref.)

77-4225 **1,3,7,9-Tetramethyluric Acid--A Chromosome-Damaging Agent Occurring as a Natural Metabolite in Certain Caffeine-producing Plants.** (Eng.) Kihlman, B. A. (Dept. Genetics and Plant Breeding, Agricultural Coll., Box 7003, S-750 07, Uppsala 7, Sweden) *Mutat Res* 39(3/4): 297-315; 1977.

The chemistry and the physiological, biochemical, physiochemical and genetic effects of 1,3,7,9-tetramethyluric acid are reviewed. Although this compound is a natural metabolite of caffeine-producing plants, it is not found in the seeds of coffee plants. Its presence in tea leaves needs further investigation. (42 refs.)

77-4226 **Fluoridation and Cancer (Letter to Editor).** (Eng.) Yiamouyiannis, J. (Natl. Health Federation, Delaware, OH 43015) Doll, R. *Lancet* 2(8032): 296; 1977.

Several errors in a report on the use of fluoridated and nonfluoridated water in various cities and cancer death rate are mentioned. Although the figures in the original article are not exact, they are fairly representative, considering the shortcomings in the data. (4 refs.)

77-4227 **Some Aspects of the Basic Mechanisms of Chemical Carcinogenesis.** (Eng.) Ts'o, P. O. (Div. Biophysics Sch. Hygiene and Public Health, Johns Hopkins Univ., Baltimore, MD 21205) *J Toxicol Environ Health* 2(6): 1305-1315; 1977.

Current research in the following areas is discussed: (1) the involvement of free radicals in benzo(a)pyrene (BP) metabolism and carcinogenesis; (2) the relationship between neoplastic transformation and somatic mutation in cultured Syrian hamster embryo (SHE) cells; and (3) comparison of DNA sequence organization and gene expression between normal and transformed SHE cells. The highly tumorigenic BP6T cell line of SHE cells has a modal chromosomal distribution of 40 (compared to 44 in untransformed SHE cells) and has lost about 5%-10% of the normal cell DNA content. Reassociation kinetics of tumor cell DNA indicate that there is a loss of DNA sequences in the single-copy family. However, hybridization with the polysomal poly(A)-messenger RNA (mRNA) of both normal SHE and BP6T cells demonstrated a great similarity in the complement of these species. No more than 4% of an estimated 12,500 mRNA's are different between the normal and transformed cells. Thus, the maintenance of malignant transformation can be accomplished by only small changes in the number of polysome-associated poly(A)-mRNA sequences. Massive gene activation is not needed. (53 refs.)

77-4228 **CHORD Operators for Cell-survival Models and Insult Assessment to Active Bone Marrow.** (Eng.) Jones, T. D. (Health Physics Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830) *Radiat Res* 71(2): 269-283; 1977.

The use of Critical Human Organ Radiation Dosimetry (CHORD) for the calculation of radiation dose to the bone marrow is discussed. This technique allows rapid estimation of insult to a nucleus, cell, organ or organism and avoids some of the pitfalls of relating risk to instrument readings. (29 refs.)

77-4229 **The Puzzle of Absent Effects.** (Eng.) Rotblat, J. (No affiliation given) *New Sci* 75(1066): 475-476; 1977.

The populations surviving the nuclear attacks at Hiroshima and Nagasaki were compared with groups who received radiation from other sources. There was a dose-related increase in the incidence of leukemia and in thyroid, breast, and lung cancer among the atomic bomb victims. However, certain other radiation effects, such as an increase in genetic effects or malignancies after exposure in utero and an increase in overall mortality from causes other than cancer, were absent. (no refs.)

77-4230 **Hiroshima and Nagasaki: The Survivors.** (Eng.) Barnaby, F. (Stockholm International Peace Res. Inst., Stockholm, Sweden) *New Sci* 25(1066): 472-475; 1977.

An international group of scientists investigated the effects of atomic radiation on the survivors of Hiroshima and Nagasaki. The incidence and mortality rates of leukemia reached a level that was 30 times higher than that of nonexposed Japanese. The incidence of thyroid, breast, lung, salivary gland, bone, and prostate cancer continues to be elevated in the exposed populace. (no refs.)

77-4231 **Radiobiological Effects of Low Doses. Implications for Radiological Protection.** (Eng.) Upton, A. C. (Dept. Pathology, State Univ. New York at Stony Brook, Stony Brook, NY 11794) *Radiat Res* 71(1): 51-74; 1977.

The biological effectiveness of a given dose of ionizing radiation may vary with the dose, dose rate, and linear energy transfer (LET) of the radiation. The implications of these variations for radiological protection are considered, with particular reference to radiobiological effects at low doses. In the induction of mutations, chromosome aberrations, cell killing, teratogenic effects, and neoplasms, the effectiveness per rad of low-LET radiation is reduced at low doses and low dose rates, but that of high-LET radiation is less dose and dose rate dependent. Dose-response patterns have been observed for carcinogenic and life-shortening effects in experimental animals. For carcinogenic effects, however, the relationships differ quantitatively and qualitatively from one type of neoplasm to another. Interpretation of the existing curves and their extrapolation to low dose rates are complicated by the multistage and multifactorial nature of the pathogenesis of neoplasms. For carcinogenic effects in humans, the data are not inconsistent with those observed in animals. However, linearity should not be excluded as a basis for estimating the risks of carcinogenic effects to low-LET radiation in certain organs and under certain irradiation conditions, although most evidence favors a nonlinear dose-effect relationship for carcinogenic effects. (64 refs.)

77-4232 **Integration of Adenovirus DNA into the Host Genome.** (Eng.) Doerfler, W. (Inst. Genetics, Univ. Cologne, Cologne, W. Germany) Baczko, K.; Burger, H.; Fanning, E.; Groneberg, J.; Ortin, J.; Scheidtmann, K. H.; Schick, J.; Soboll, H. *Bull Inst Pasteur* 75(2): 141-185; 1977.

A comprehensive review is presented of the biology of the adenoviruses (ADV) and of the integration of ADV-DNA into host genomes. Discussion is made of the structure, polypeptide composition, core, and DNA of the ADV virion; productive, abortive, and semipermissive infection and transformation in ADV-host cell systems; and the integration of ADV-DNA into the genome of productively infected, abortively infected, and transformed cells. (219 refs.)

77-4233 **Rejectability of Virus-induced Tumors and Nonrejectability of Spontaneous Tumors--A Lesson in Contrasts.** (Eng.) Klein, G. (Dept. Tumor Biology, Karolinska Inst., Stockholm, Sweden) Klein, E. *Isr J Med Sci* 13(7): 666-676; 1977.

Experimental evidence concerning the ineffectiveness of host immune defenses against the development of spontaneous tumors is discussed. The "central fallacy of tumor immunology" is defined to be: "All tumors are potentially recognized by the host immune response. Tumor development is therefore always a breakdown of the response. Therapy must strive to correct the breakdown." Two explanations, contrary to the "breakdown of response" hypothesis, are proposed to account for the poor rejectability of spontaneous tumors: (1) during tumor progression, the evolving clones are selected for decreased immunogenicity; (2) host immune defenses against tumor-specific antigens of spontaneous tumors have not been strengthened by natural selection because these tumors arise principally in old age, after most of the reproductive potential of the individual has been realized. Advantageous mutations can not therefore be "fixed" into the gene pool of the general population. (61 refs.)

77-4234 **Addition of Extra DNA Sequences to Simian Virus 40 DNA In Vivo.** (Eng.) Yoshiike, K. (Dept. Enteroviruses, Natl. Inst. Health, Kamiosaki, Shinagawa-ku, Tokyo 141, Japan) Defendi, V. *J Virol* 23(2): 323-337; 1977.

The possible addition of extra sequences to simian virus 40 (SV40) DNA was analyzed by electron microscopy in two different cell systems: productively infected monkey cells and activated heterokaryons of monkey and transformed mouse 3T3 cells. The closed circular DNA fraction, extracted from monkey cells at 70 hr after infection with nondefective SV40 at a multiplicity of infection of 6 plaque-forming units/cell, contained oversized molecules (1.1-2.0 fractional lengths of SV40 DNA) constituting about 8% of the molecules having lengths equal to or shorter than SV40 dimer DNA. The oversized molecules had the entire SV40 sequences. The added DNA was heterogeneous in length, and the sites of addition were not specific with reference to the EcoRI site. These results suggest that recombination between monkey and SV40 DNA's or partial duplication of SV40 DNA occurs at many sites on the SV40 chromosome. The integrated SV40 DNA is excised and replicates in activated heterokaryons. In this system, heterogeneous undersized and oversized molecules containing SV40 sequences in the closed circular DNA population were also found. Additions differing in size appeared to be overlapping and to have occurred at a preferential site on the SV40 chromosome. These results support the hypothesis that host DNA can be added to SV40 DNA at the site of integration at the time of excision. (21 refs.)

77-4235 **Viral Messenger Structures: Some Surprising New Developments.** (Eng.) Marx, J. L. (No affiliation given) *Science* 197(4306): 853-855, 923; 1977.

In recent investigations, it was found that certain messenger RNA's synthesized by adenovirus 2 and simian virus 40 (SV40) consist of contiguous segments coded for by widely separate portions of the viral DNA. The findings may apply to at least some of the animal cells in which the viruses multiply. (no refs.)

77-4236 **Cell Transformation with Herpes Simplex Viruses.** (Eng.) Portugal, F. H. (No affiliation given) *Nature* 269(5625): 196; 1977.

Studies with herpes simplex virus fragments have indicated that some fragments, coding for certain biochemical functions, can transform mammalian cells. Further studies will help shed light on the viral etiology of oncogenic transformation. (7 refs.)

77-4237 **Structure of the Intermediates Leading to the Integrated Provirus.** (Eng.) Weinberg, R. A. (Center Cancer Res., Massachusetts Inst. Technology, Cambridge, MA 02139) *Biochim Biophys Acta* 473(1): 39-55; 1977.

Current knowledge of the mechanisms by which retroviruses transfer their genetic information from the single-stranded RNA of their virions to a double-stranded DNA linked to the cellular genome is surveyed. It is believed that in vivo reverse transcription of the single-stranded RNA begins near the 5′-end, progresses a short distance to the 5′-end, and then continues at the 3′-end of the same or another RNA subunit. This association of the initially synthesized DNA with both ends of the RNA template may lead to a transient circular form, the ends of the RNA being linked by DNA. The consequence of these initial steps is a DNA molecule, of length comparable to the viral genome, which may only have a transient association with the RNA on which it was synthesized. By unknown mechanisms, a double-stranded linear DNA molecule of full genome length is next synthesized. This form of the DNA is infectious and may have "sticky ends", in that it appears to circularize at high ionic strength. It may be the immediate precursor of the integrated form of the virus. (84 refs.)

77-4238 **The Role of IgE in the Immune Response to Neoplasia: A Review.** (Eng.) Rosenbaum, J. T. (Dept. Medicine, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT 06510) Dwyer, J. M. *Cancer* 39(1): 11-20; 1977.

The role of IgE in the immune response to neoplasia has received little attention, despite suggestive evidence for an IgE response to tumor-specific antigens. A complex interrelationship exists among basophils, eosinophils, histamine, complement, and T cells. The latter cells play a central role in the immune response to neoplasia and, in addition, are now considered important in the production and regulation of IgE, the molecule that may supply an important link between the pharmacological and cellular dynamics of a successful antitumor response. The evidence for an IgE role in the immune response to tumors, the relationship between atopy and cancer, and the possible mechanisms by which IgE could enhance tumor rejection are discussed. (138 refs.)

77-4239 **Immunology and Immunotherapy of Human Tumors.** (Eng.) Harris, J. E. *In: The Immunology of Malignant Disease.* (St. Louis: C. V. Mosby Co.) 2nd ed., pp. 410-579; 1976.

Investigations of immunology and immunotherapy are reviewed following an introductory consideration of the etiology of human tumors. Evidence suggests a viral etiology for leukemias, lymphomas, sarcomas, and bladder, nasopharyngeal, and cervical carcinomas. Immune defects may also be causative factors in human malignancy, as evidenced by the increased risk of tumor development following congenital immune deficiencies, collagen diseases, benign lymphoproliferative diseases, or immune suppression in transplant recipients. Immunologic factors and their application to immunotherapy in specific malignant diseases are discussed extensively. The local and regional efficiency of nonspecific immunostimulation has been documented best against skin tumors, malignant melanoma, and bladder carcinoma. Systemic nonspecific immunostimulation significantly improved the prognosis of acute myelogenous leukemia; other tumors (malignant melanoma, breast and colon carcinoma, and malignant lymphoma) also benefitted from this type of immunotherapy. The herpesviruses are strong candidates as causative agents of some human tumors, but effective herpesvirus vaccines have not yet been prepared for any human tumor. However, it is suggested that vaccination against Burkitt's lymphoma and nasopharyngeal carcinoma should be given consideration for the well-identified high-risk groups. Preventive oncornavirus vaccines could possibly also be considered for persons with high risks of leukemia and breast carcinoma. (1509 refs.)

77-4240 **Role of Immunological Factors in Cancer Susceptibility.** (Eng.) Gatti, R. A. (Div. Pediatric Oncology and Immunology, Cedars-Sinai Medical Center, Los Angeles, CA 90048) *Prog Cancer Res Ther* 3: 329-338; 1977.

Data suggest that immunosurveillance does play a role in the oncogenesis of some tumors and that it may be difficult to separate, in vivo, (1) the effects of most carcinogens on basic intercellular mechanisms leading to malignant transformation from (2) the effects that produce host immunosuppression. Faulty immunosurveillance is probably not the sole or even primary cause of oncogenesis; more likely is a multifactorial hypothetical model of oncogenesis. Briefly, certain genetic backgrounds may predispose a host to certain viruses or other carcinogens; however, the two must be paired appropriately, since certain carcinogens have little or no effect on some hosts. A target cell is transformed and it begins to multiply, during which time it may be influenced by hormones, poietins, microenvironments, and other mechanisms of development and differentiation. Leukemogenesis in mice has been linked to the major histocompatibility locus (H-2), but other genes are also involved in this process that are not associated with the H-2 area. Most likely, the HLA locus in man is homologous to the major histocompatibility areas of other species. This homology predicts that cancer susceptibility genes are more likely to be located in the proximity of HLA-D than near either the HLA-A or -B loci. There is a new methodology for defining the HLA-D locus that involves the use of established lymphoblastoid cell lines from D-locus homozygous donors as stimulators in mixed WBC cultures. A panel of 35 typing lines has been established and frozen in typing plates. (14 refs.)

77-4241 **Genetic and Environmental Interactions in the Origin of Human Cancer.** (Eng.) Knudson, A. G. (Graduate Sch. Biomedical Sciences, Univ. Texas Health Science Center, Houston, TX 77030) *Prog Cancer Res Ther* 3: 391-399; 1977.

The increase in age-specific incidence for most cancers follows a distinct pattern that is a simple power function of time. Tumor production is also time-dependent in instances in which a dominant gene strongly predisposes its host to cancer, as in polyposis of the colon. The slopes of the curves, however, are not the same. The combination of earlier onset and multiplicity is typical for dominantly inherited tumors, as is time-dependence. Two conclusions can be drawn: (1) Mendelian genes can create a high probability for development of a tissue-specific tumor in the host, and (2) at the cell level, tumor production is a rare event whose probability of occurrence increases with time. The inherited mutation itself does not cause cancer. A minimal requirement for any model of carcinogenesis is one that allows for two mutation events, one that can be either germinal or somatic, the other somatic. Environmental agents may increase these mutation rates and, therefore, the probability that cancer will occur. However, the action of these agents may in turn be influenced by the genetic constitution of the host. Also, one of the mutational steps can be acquired prezygotically and the rate of occurrence of that germinal mutation may be increased by environmental mutagens. The interactions of genetic and environmental factors are shown schematically. In conclusion, the multitude of cancers may be a set of single gene disorders resulting from a complex interaction of spontaneous mutation, physiological and genetic modulation, and environmental agents. (19 refs.)

77-4242 **Clinical Genetics and Cancer.** (Eng.) Opitz, J. M. (Clinical Genetics Center, Dept. Medical Genetics, Univ. Wisconsin, Madison, WI 53706) Herrmann, J. *Prog Cancer Res Ther* 3: 465-474; 1977.

Clinical genetics involves clinical and diagnostic activities, genetic analysis, and genetic counseling. An outline of the methods of genetic nosology is presented. Numerous insights can be expected from applying nosologic methods to genetic and congenital disorders, including those with neoplastic features. They should lead to better understanding of the natural history of cancer, the action of different environmental causes, the action of different mutant genes and classes of mutant genes, and the delineation of new syndromes (S's) and, ultimately, their cause. Four groups of S's and genetic disorders are characterized: deformities and deformity S's (Potter S, the arthrogryposes, etc.), malformations and malformation S's, dysplasia and polydysplasia S's, and inborn errors of metabolism and metabolic diseases. Several conditions share the characteristics of more than one group. In general, single congenital anomalies (developmental field complexes, DFC's) and most multiple congenital anomaly (MCA) S's are not associated with an increased risk of neoplasia. However, there are several exceptions. Among those listed are the Wilms' tumor-leukemia/aplastic anemia S, the renal malformation-Wilms' tumor association, Poland anomaly-leukemia association, the diGeorge S or DFS-lymphoma association, chromosome imbalance S's, Fanconi MCA/anemia S, aniridia-Wilms' tumor S, nevoid basal cell carcinoma S, hemihypertrophy-Wilms' tumor association, and the Wiedemann-Beckwith S. (21 refs.)

77-4243 **Genetic Markers and Cancer.** (Eng.) King, M. C. (G. W. Hooper Foundation, Univ. California Sch. Medicine, San Francisco, CA 94143) Petrakis, N. L. *Prog Cancer Res Ther* 3: 281-290; 1977.

The use of genetic markers to define groups at high risk for cancer is reviewed. A genetic marker constitutes a protein or other phenotype determined by a single locus with two or more alleles present at significant frequencies in a certain population. Genetic markers can contribute to two genetic-epidemiologic approaches to the study of cancer. First, allelic frequencies at the marker locus may differ in cancer subjects compared with healthy subjects. Studies of associations between genetic markers and disease have been the most common use of genetic markers in cancer epidemiology. Examples are (1) the possible causal relationship between breast cancer and the cerumen marker, and (2) the use of the Duffy blood group to determine whether black cancer patients have genotypes derived in greater measure from Caucasian (rather than African) ancestry more frequently than healthy black persons. A second approach is linkage analysis, which investigates whether loci are closely linked physically on the same chromosome so that they are inherited together in families. To be useful for either association or linkage analysis, potential marker genes should produce traits that are clearly defined manifestations of single loci. A third approach involves combining multiple genetic markers and more traditional epidemiologic (environmental) parameters to determine a constellation of factors defining a high-risk group. The goal of this approach is to accurately assign asymptomatic persons in a given age, sex, ethnic, and socioeconomic group to a high- or low-cancer-risk group. (43 refs.)

77-4244 **Genetics and Etiology of Human Cancer.** (Eng.) Knudson, A. G. (Univ. Texas Health Science Center, Houston, TX 77030) *In: Advances in Human Genetics.* Harris, H.; Hirschhorn, K., eds. (New York: Plenum Press) pp. 1-66; 1977.

This review of genetic states associated with cancer includes a discussion of chromosomal abnormalities, mutagenic disorders and associated pathology, immunodeficiency disorders, dominant conditions such as polyposis syndromes, common adult tumors linked to chromosomal aberrations, and pediatric malignancies such as leukemia and lymphoma, which can have a genetic predisposition. (320 refs.)

77-4245 **Is There a Scientific Basis for Six-monthly Dental Examinations?** (Eng.) Sheiham, A. (Dept. Community Dental Health, London Hosp. Medical Coll. Dental Sch., Turner St., London E1 2AD, England) *Lancet* 2(8035): 442-444; 1977.

The 6-mo interval between dental examinations was found to be unnecessary for the detection of oral malignancies. The risk of cancer in the oral cavity is small; oral cancer is easily detected and biopsied, and, because of its rarity, suspicious cases should be referred to qualified practitioners. Other aspects of the 6-mo period between evaluations are reviewed. (41 refs.)

77-4246 **Red-brown Pigment May Cause Skin Cancer.** (Eng.) Anonymous (No affiliation given) *Chem Eng News* 55(38): 5; 1977.

Pheomelanin, a red-brown pigment in the hair and skin of persons with red hair, was found to be mutagenic in one run of the Ames test. Further studies are necessary to find the compound that is causing the positive result and how, if at all, it could be carcinogenic in man. Preliminary studies indicate that the compound may be broken down before it can have any influence. (1 ref.)

77-4247 **Bone.** (Eng.) Geschickter, C. F.; Copeland, M. M. *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 728-750; 1976.

The diagnosis and management of bone cancer patients are discussed. Malignant cartilaginous growths are usually secondary to benign osteochondromas or enchondromas and are prone to occur in adults. A primary malignant periosteal cartilaginous growth in childhood or adolescence is a highly malignant sarcoma that requires prompt amputation. Hereditary skeletal dysplasias (multiple exostosis, multiple enchondromatosis, and Maffucci's syndrome) may be complicated by chondrosarcoma, which is similar to the sarcoma secondary to solitary exostosis or solitary chondromas. Malignant chondroblastomas are rare and can be differentiated from the benign type only by histopathologic study. These patients succumb to pulmonary metastasis. Osteogenic sarcoma is a malignant tumor of a single bone affecting adolescents. Ewing's sarcoma, a highly malignant tumor that occurs in bone but is incapable of producing bone, affects children between 5-12 yr old. A subvariety of Ewing's sarcoma, reticulum cell sarcoma of bone, occurs in young adults. Both tend to metastasize to other bones. Multiple myeloma nearly always presents with the characteristic features of multifocal involvement of the red marrow-containing bones with elevated serum proteins, severe back pain, and anemia. Metastatic skeletal involvement by malignant tumors arising elsewhere occurs most frequently in patients with mammary, prostatic, renal, or pulmonary carcinoma. The major forms of malignant disease involving the bones of children include neuroblastomas, leukemia, Wilms' tumor of the kidney, and sacroccygeal neoplasms. Children with bone involvement rarely survive for long periods of time and they require aggressive combined therapy. (14 refs.)

77-4248 **How Does Leukemia Invade the CNS?** (Eng.) Pochedly, C. (Dept. Pediatric Hematology, Nassau County Medical Center, East Meadow, NY) *In: Leukemia and Lymphoma in the Nervous System. Pochedly, C., ed. (Springfield, IL: Charles C. Thomas):* pp. 54-67; 1977.

Successful chemotherapy of acute leukemia has resulted in a marked increase in the incidence of CNS leukemia. Leukemic cells in the CNS may arise from a number of sources:

(1) by direct extension from the bone marrow through the dura; (2) by hematogenous spread or metastasis from extracranial bone marrow; (3) by spread through lymphatic channels; and (4) de novo in the choroid plexus or in the walls of the arachnoid veins. The evidence from chromosomal studies and leukemic lymphosarcoma studies and the correlation with peripheral blood findings indicate a metastatic origin from the bone marrow for most cases of CNS leukemia. Experimental studies with L1210 leukemia in mice support the concept that increased incidence of CNS leukemia correlates with prolonged survival. Leukemic cells probably continue to proliferate in the CNS while the bone marrow and peripheral blood show complete remission because of the failure of chemotherapeutic agents to cross the blood-brain barrier. This permits leukemic cells in the CNS to live in a protected environment. Immunological and pharmacological barriers that foster the growth of foci of leukemic cells during systemic remissions may also exist in the CNS. (23 refs.)

77-4249 **The Adrenal Glands.** (Eng.) Newsome, H. H. (Medical Coll. Virginia Hosp., Richmond, VA) Kay, S.; Lawrence, W. *In: Management of the Patient with Cancer. 2nd ed.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.): 2nd ed., pp. 700-727; 1976.

Signs and symptoms, diagnostic modalities, and treatment of neoplasms of the adrenal cortex, primary aldosteronism due to adrenocortical carcinoma, and pheochromocytoma are covered. Patients with nonfunctioning adrenocortical carcinomas usually present with abdominal pain or an abdominal mass, while those with functioning adrenocortical carcinomas present with a myriad of symptoms reflecting the underlying type of hormonal excess. Usually, these tumors produce Cushing's syndrome with varying degrees of virilization. Cortical neoplasms are diagnosed by measuring free urinary cortisol excretion, the high-dose dexamethasone test, the metapyrone test, and ACTH infusion. Carcinoma of the adrenal cortex causing primary aldosteronism is rare. These tumors are usually very large, even in the kilogram range. These patients present with debilitating weakness, severe hypertension, and hypokalemic alkalosis. Diagnosis rests on the demonstration of an elevated rate of aldosterone secretion. The large malignant tumors can be readily detected by arteriography. The incidence of pheochromocytoma is $< 1\%$ of all hypertensive patients. In appearance it is a well-delineated, circumscribed tumor. A functioning pheochromocytoma is diagnosed by an increased secretion of catecholamines or their metabolic products. (90 refs.)

77-4250 **Some Ultrastructural Aspects of Experimental and Human Carcinoma of the Bladder.** (Eng.) Koss, L. G. (Dept. Pathology, Albert Einstein Coll. Medicine at Montefiore Hosp. and Medical Center, Bronx, NY 10467) *Cancer Res* 37(8, part 2): 2824-2835; 1977.

Data from transmission electron microscopy studies of the structure of normal rat bladder epithelium and of chemically induced experimental bladder carcinoma in female Fischer 344 rats are reviewed. Similar studies in man are also reviewed briefly. Metabolites of cyclophosphamide (CP) are very toxic to the urothelium, and a single ip dose (5-200 mg/kg) may produce extensive epithelial necrosis in a variety of experimental animals and in man. Epithelial events during carcinogenesis induced by CP and several other agents in rats are discussed in terms of sequential changes in cell-to-cell relationships, the asymmetric unit membrane (a cell marker that is a functional end stage of epithelial differentiation), the Golgi apparatus, and keratinization. Nonepithelial events related to the lamina densa of the basement membrane and the subepithelial capillary vessels are also described. Many of the changes may reflect rapid epithelial growth and turnover rather than specific morphological expressions of carcinogenesis. However, the early injury to the Golgi apparatus and the occurrence of microvilli on the cell surfaces cannot be so explained and may represent a more specific morphological response to the carcinogen. Squamous metaplasia was considered a possible factor in the formation of invasive carcinoma. Observations on normal human bladder, urothelial hyperplasia, and papillary tumors are insufficiently documented to allow more than a preliminary statement. Similarities with the experimental systems were noted. The significance of these observations was discussed in terms of Carins' theory of epithelial carcinogenesis. (68 refs.)

77-4251 **The Lung, the Trachea and the Pleura.** (Eng.) Nealon, T. F. (Dept. Surgery, St. Vincent's Hosp. and Medical Center New York, New York, NY) Ching, N. P. *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 309-333; 1976.

Bronchogenic carcinoma is one of the major causes of death from cancer and is primarily a disease of men. A direct relationship between cancer of the lung and smoking is suggested by recent studies. The three main histologic types of bronchogenic carcinoma are epidermoid, anaplastic, and adenocarcinoma, in order of frequency. The most malignant type is the anaplastic small cell (oat cell) carcinoma. Symptoms of lung cancer include cough, high temperature and cough, wheezing, and hoarseness. X-ray of the chest is the most important examination available for detecting this cancer, followed by bronchoscopy, cytology, and mediastinoscopy. Cancer of the trachea is rare, with the commonest lesion being squamous cell carcinoma. Early symptoms are cough and dyspnea. Later symptoms include wheezing, dysphagia, and hoarseness. Bronchoscopy is the best means of establishing the diagnosis and histologic type. The predominant primary malignant tumor of the pleura is diffuse multiple mesothelioma. Symptoms include severe chest pain followed by dyspnea, as fluid accumulates, and wt loss. X-ray of the chest is helpful in establishing a diagnosis. There seems to be two variants. The more malignant form is characterized by large nodules, a more malignant histology, and a fulminating course lasting only a few months. The other form produces only tiny nodules, a more orderly histology, and a course of 1-2 yr. (71 refs.)

77-4252 **The Larynx.** (Eng.) Ogura, J. H. (Dept. Otolaryngology, Washington Univ. Sch. Medicine, St. Louis, MO) Spector, G. J. *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 206-238; 1976.

Laryngeal cancer comprises 2%-5% of all malignancies diagnosed annually. Smoking and excessive alcohol intake are frequently associated with laryngeal and laryngopharyngeal cancers. Herpes simplex infections have been implicated as predisposing to laryngeal cancer, as have leukoplakia and keratosis of the vocal chords, chronic infections and irritations, irradiation, and air pollution. Squamous cell carcinomas account for 95%-98% of all malignant neoplasms of the larynx. Sarcomas comprise the majority of other tumors, and they have a greater incidence of metastasis than squamous cell carcinoma. Metastasis to the larynx is common, with the primary site being renal cell, prostate, breast, or metastatic melanoma. Hoarseness is the primary symptom of laryngeal carcinoma. Dyspnea and stridor are late symptoms caused by airway obstruction. Pain, dysphagia, cough, and hemoptysis are also seen. There are two groups of signs of laryngeal carcinoma: (1) those found on neck examination, such as a lump in the neck, broadening or tenderness of the larynx, loss of crepitation, and fullness in the thyrohyoid membrane; and (2) those seen by visualization of the larynx. Five of the following six methods of examining the larynx are required for a complete diagnostic examination: (1) palpation; (2) indirect mirror examination; (3) direct laryngoscopy; (4) plain radiography; (5) polytomography or laminography of the larynx; and (6) contrast study of the larynx. The most important factors influencing survival are location and size of the primary lesion, cellular differentiation, and cervical metastasis. Metastasis to the cervical lymph nodes carries the poorest prognosis. (84 refs.)

77-4253 **The Cervix.** (Eng.) Nelson, J. H. (State Univ. Hosp., Kings County Hosp. Center, Brooklyn, NY) Nikrui, N. *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 658-673; 1976.

The etiology, pathology, symptoms, signs, diagnosis, and treatment of cancer of the cervix are discussed. Cervical cancer occurs almost exclusively in women who have had sexual experience, especially in those who have had early sexual activity and in those who have been promiscuous. Another possible etiological factor is herpesvirus type 2. Almost all cases of cervical malignancy occur as either squamous cell carcinoma or adenocarcinoma. Carcinoma in situ is a precursor of invasive carcinoma. Adenosis (a benign lesion occurring in the vaginal wall) is often found in adolescent girls with a history of maternal stilbestrol ingestion during pregnancy. In a small number of cases, this lesion undergoes malignant transformation. The precursor lesions of carcinoma are not likely to cause symptoms. Symptoms of invasive carcinoma of the cervix include vaginal discharge, postcoital bleeding, and intermenstrual bleeding. Pain is a late manifestation. In most cases no physical signs will be present. The Papanicolaou examination of cervical smears is the only effective cancer detection method available today. Colposcopy and biopsy aid in the diagnosis of patients with an abnormal cytologic report. (18 refs.)

77-4254 **The Endometrium.** (Eng.) Barber, H. R. (New York Hosp., New York, NY) Kwon, T. H. *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 641-657; 1976.

The predisposing factors, symptoms, diagnosis, pathology, and treatment of endometrial cancer are discussed. Several parameters are associated with this disease; ie, obesity, nulliparity, reduced glucose tolerance, hypertension, hyperestrogenism, continuous uninterrupted estrogen stimulation, menses continuing beyond age 50, a history of dysfunctional uterine bleeding, and a history of anovulation. The first and most important symptom is abnormal bleeding. The comparative accuracy of the techniques for detecting endometrial cancer is as follows: vaginal pool, 50%; ectocervical sampling, 70%; endometrial brush technique, 75%; uterine aspiration smears, 80%; intrauterine lavage, 87%; and Gravelee jet washer, 93%. About 40% of endometrial cancers are circumscribed. The diffuse type involves most of the endometrium and is characterized by its rough granular growth. Cancer arising in the endometrium tends to remain within the uterus for a long time, spreading by local extension within the endometrium. It also spreads through the lymphatic system. Patients at high risk for extrauterine spread are those with involvement of the lower uterus or cervix, Grade III lesions, and myometrial invasion. (35 refs.)

77-4255 **Hysterectomy and Sterilization: Changes of Fashion and Mind.** (Eng.) Anonymous (No affiliation given) *Br Med J* 2(6089): 715-716; 1977.

Since sterilized patients have a higher than normal risk reported for the development of endometrial cancer, perhaps hysterectomy should be considered as the initial means of sterilization. Other changing attitudes regarding hysterectomy and sterilization are discussed. (9 refs.)

77-4256 **The Colon.** (Eng.) Rhoads, J. E. (Dept. Surgery, Univ. Pennsylvania Sch. Medicine, Philadelphia, PA) Mackie, J. A. *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 524-541; 1976.

Malignant tumors of the colon and rectum, the most frequent form of malignancy in the US after skin cancer, are discussed. Familial multiple polyposis, villous and adenomatous polyps, and ulcerative colitis predispose to the development of carcinoma of the colon. The usual adenocarcinoma of the large bowel is a bulky tumor with well-defined edges surrounding a central ulcerated area; the usual carcinoma is a well-differentiated tumor. The more poorly differentiated, anaplastic tumors generally are more malignant and more invasive. Carcinoma of the colon limited to the bowel wall without lymph node metastasis has a good prognosis when adequately excised. Extension beyond the serosa of the bowel wall may lead to the implantation of tumor cells in adjacent structures. Carcinomas of the cecum are less invasive and have a lower percentage of lymph node metastasis than those of the rectum and rectosigmoid. Operative mortality tends to be higher in the older, poor-risk patients, particularly when they present with an intestinal obstruction. Survival for 5 yr following resection of the colon is 34% with lymph node metastasis and 68% without. Other malignant tumors that are occasionally seen in the colon are fibrosarcomas, leiomyosarcomas, lymphosarcomas, hemangiopericytomas, carcinoids, and squamous cell carcinomas. About 10% of carcinoids of the rectum are malignant. Carcinoids should be excised because of their malignant potential and because they produce symptoms. (33 refs.)

77-4257 **Ureterosigmoidostomy and Neoplasia (Letter to Editor).** (Eng.) Koster, L. H. (502 Fifth St., New Kensington, PA 15068) Antoon, S. J. *Urology* 10(3): 290; 1977.

The high incidence of colon carcinoma in patients who have undergone ureterosigmoidostomy necessitates a life-long followup. Neoplasia has been discovered from 7-46 yr post-diversion. Two cases involved fatal metastases. (2 refs.)

77-4258 **The Small Bowel.** (Eng.) McPeak, C. J. (Gastric and Mixed Tumor Service, Memorial Hosp., New York, NY) *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 502-517; 1976.

Cancer of the small bowel, including its incidence, pathology, symptoms, diagnosis, and treatment, is considered. The incidence of these tumors is relatively low but they are not rare, comprising from <1% to >5% of gastrointestinal neoplasms in various series. Primary malignant tumors of the small intestine fall into three major categories: (1) carcinomas, arising from the mucosal surface; (2) leiomyosarcomas, arising from the smooth musculature; and (3) tumors of lymphatic origin. The most characteristic symptoms are intermittent intestinal obstruction with cramping pains in the periumbilical region or the lower abdomen. The characteristic symptomatology has been classified into the anemic, obstructive, and perforative syndromes. The barium contrast meal is the most valuable x-ray diagnostic study for detecting these tumors. (77 refs.)

77-4259 **The Stomach.** (Eng.) Nealon, T. F. (Dept. Surgery, St. Vincent's Hosp. and Medical Center New York, New York, NY) *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 413-450; 1976.

The epidemiology, symptoms and signs, diagnosis, and treatment of cancer of the stomach are discussed. The rates for white people in the US are the lowest in all countries with a death registration system. Countries and areas farthest from the equator seem to have the highest rates. There is some familial tendency toward gastric cancer. Pernicious anemia, achlorhydria, and hypochlorhydria are all associated with a high occurrence of gastric cancer. The relationship of carcinoma with chronic gastritis and chronic gastric ulcer is controversial, but it is believed that benign chronic gastric ulcers show definite malignant transformation in a small number of patients. Gastric carcinoma may also arise 8-25 yr after gastroenterostomy or gastrectomy for benign peptic ulcer. Gastric carcinoma is divided grossly into three types: (1) fungating carcinoma; (2) ulcerating carcinoma; and (3) diffuse or infiltrating carcinoma. Histologically, it is divided into four classifications: (1) carcinoma in situ; (2) adenocarcinoma; (3) gelatinous or mucoid carcinoma; and (4) metaplasia (squamous cell cancer or choriocarcinoma). Metastasis occurs most frequently in the lymphatics, liver, lung, muscle, and brain, in that order. Occasionally, gastric symptoms suggesting intrinsic malignant disease are due to secondary invasion of the stomach from a primary lesion elsewhere. Three general types of symptoms are usually observed: the anemia syndrome, the peptic ulcer syndrome, and symptoms of vague indigestion. Gastric x-ray studies are the most important diagnostic procedure, followed by gastroscopy, cytology, esophagoscopy, and exploratory laparotomy. (117 refs.)

77-4260 **Melanoma.** (Eng.) Booher, R. J. (Gastric and Mixed Tumor Service, Memorial Hosp., New York, NY) McPeak, C. J. *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 117-159; 1977.

The histiogenesis, classification, incidence, pathology, diagnosis, and treatment of malignant melanoma are reviewed. There is controversy over whether the melanoblast or melanocyte is of neuroectodermal or epidermal origin. Melanomas capable of metastasis are extremely rare in children, but any pigmented lesion that is rapidly growing, ulcerated, or darkly pigmented or changes in color should be excised for diagnostic certainty. Melanoma comprises approx 1% of the cancers in both sexes, excluding nonmelanoma skin cancer and carcinoma in situ of the uterine cervix. Melanoma is seen most often in the fifth and sixth decades of life and in light-complexioned, sandy-haired, freckled individuals who do not tan. There is a general consensus that nevus precedes melanoma in about 64% of the patients. About 40% will enjoy local control of their melanoma and will remain cured. The prognosis depends on the absence or presence of metastases in the lymph nodes at the time of operation. Lymphangiography has been used as a supplement to clinical evaluation of regional lymph nodes. The principle of wide excision of a primary melanoma and incontinuity dissection of regional nodes is widely accepted. (222 refs.)

77-4261 **The Skin.** (Eng.) Hugo, N. E. (Lakeside Veterans Admin. Hosp., Chicago, IL) *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.) 2nd ed., pp. 83-116; 1976.

The incidence, etiology, signs and symptoms, diagnosis, and treatment of skin cancer are discussed. A survey by the National Cancer Institute indicates that there are about 300,000 cases of skin cancer annually, 90% of which occur on exposed areas. Sunlight is the major etiologic cause but other forms of radiation, chemicals, and irritation are also implicated. Carcinoma of the skin is classified as basal cell carcinoma or squamous cell carcinoma. Basal cell carcinoma is a localized malignancy that grows slowly and causes serious mutilation or death only in neglected cases. Squamous cell carcinoma has a more rapid growth rate, may metastasize to regional lymph nodes, and may cause death from widespread metastases. The skin may be the site of metastatic carcinoma, which presents as multiple nodules in one area of the body. Skin cancer may also appear as a direct extension of an underlying tumor. Primary carcinoma of the nasal sinuses or oral cavity may invade the skin. Marjolin's ulcer is a variation of squamous cell carcinoma that develops in scars and long-standing ulcerations following burns. Skin cancer may develop in areas of radiation dermatitis. Sebaceous carcinoma is a rare form of epidermoid carcinoma of the skin that develops in a sebaceous adenoma or gland. Multiple carcinomas of the skin may be found in 20% of cases. (230 refs.)

77-4262 **Trophoblastic Lesions.** (Eng.) Gore, H. (Rochester General Hosp., Rochester, NY) Hertig, A. T. *In: Management of the Patient with Cancer. 2nd ed* Nealon, T. F., ed. (Philadelphia: W. B. Saunders Co.): pp. 682-699; 1976.

The development of hydatidiform mole (HM), its complications, and the treatment of patients with trophoblastic disease are considered. HM develops as a segmental dilatation of chorionic villi when there is an active fetal trophoblast in contact with a functioning maternal circulation but there is no fetus-to-villus circulation. The fully developed HM is usually aborted at 17-18 wk or is suspected clinically at that time. The significant complications of HM are invasive (or metastatic) mole and choriocarcinoma. The invasive or metastatic mole results from either direct local extension or deportation of groups of molar villi without true tumor formation. Choriocarcinoma is a pure epithelial tumor that may accompany or follow any type of pregnancy. About one-third of choriocarcinomas are preceded by abortion, one-third by a pregnancy of >20 wk gestation, and one-third by HM. The most common sites of metastatic choriocarcinoma in patients who have died of the disease are lung, brain, and liver, in that order. Chorionic gonadotropin determination is the principal laboratory technique for the follow-up of patients with trophoblastic disease. Only rarely does a choriocarcinoma not produce this hormone. However, other tumors may produce chorionic gonadotropin; these include colonic, breast, bronchogenic, ovarian, and renal cell carcinomas. (91 refs.)

77-4263 **The Epidemiology of Breast Cancer.** (Eng.) Levin, M. L. (Dept. Epidemiology, Johns Hopkins Univ. Sch. Medicine, Baltimore, MD) Thomas, D. B. *In: Current Trends in the Management of Breast Cancer.* Baker, R. R., ed. (Baltimore: Johns Hopkins Univ. Press) pp. 1-20; 1977.

Risk factors associated with breast cancer are discussed. The high incidence of female breast cancer in the Western world is probably caused by environmental rather than ethnic factors, because migrants from low- to high-risk countries develop breast cancer at intermediate rates. The incidence of breast cancer rises steeply to age 50, flattens out for the next 5 yr, and then increases again. The change in the rate at the age of menopause suggests that endogenous hormones are of etiologic importance. Women whose age at first birth was ≥ 35 yr have a $>50\%$ higher risk than the general population. The risk is lower in women with late menarche and early menopause, either artificial or natural. Urinary excretion of low levels of androgen metabolites and excretion of the inactive form of these substances are associated with an increased risk. Urinary estriol excretion is associated with a decreased risk. These excretion patterns indicate endocrinologic abnormalities at the breast tissue level that may play a role in the genesis of breast cancer. Obesity and dietary fat, also positively correlated with an increased risk, may be related to breast cancer development because of associated changes in endogenous hormones. A relationship between exogenous estrogens and breast cancer has not been proved. There is evidence that an oncogenic RNA virus or high doses of ionizing radiation may be involved in the genesis of breast cancer. A relationship is suspected between fibrocystic breast disease and increased risk, as well as between treatment of hypertension with reserpine and increased risk. Oophorectomy before age 35 appears to have a protective effect. (80 refs.)

77-4264 **Different Rate-limiting Steps in Excision Repair of Ultraviolet- and N-Acetoxy-2-acetylaminofluorene-damaged DNA in Normal Human Fibroblasts.** (Eng.) Ahmed, F. E. (Biology Dept., Brookhaven Natl. Lab., Upton, NY 11973); Setlow, R. B. *Proc Natl Acad Sci USA* 74(4): 1548-1552; 1977.

Normal human fibroblasts were exposed for 20 min to various concentrations of the carcinogen N-acetoxy-2-acetylaminofluorene (AAAF) in combination with various doses of 254-nanometer UV radiation at a rate of 0.36 watt/m^2. Unscheduled DNA synthesis and sites sensitive to a UV endonuclease extracted from *Micrococcus luteus* were measured to determine if limited UV repair was affected by AAAF treatment. Combined treatment resulted in much more unscheduled DNA synthesis than the saturation level observed with UV alone at doses of 20 joules/m^2. The amount of unscheduled DNA synthesis approximated the sum of those amounts observed for each separate treatment, even at saturation doses. AAAF treatment did not inhibit the removal of pyrimidine dimers by exogenous UV endonuclease, even when AAAF concentrations were as high as 10 μM or equivalent to the UV saturation dose in terms of unscheduled DNA synthesis. Even though AAAF damage mimics UV damage, the rate-limiting steps and enzymatic pathways involved in excision repair of the two types of damge appear to be different. (30 refs.)

77-4265 **Differences in Removal of Acetylaminofluorene and Pyrimidine Dimers from the DNA of Cultured Mammalian Cells.** (Eng.) Amacher, D. E. (Pfizer Central Res., Groton, CT 06340); Elliott, J. A.; Lieberman, M. W. *Proc Natl Acad Sci USA* 74(4): 1553-1557; 1977.

A variety of confluent cultured mammalian cells were exposed to either UV light (10-20 joules/m^2) or the carcinogen N-acetoxy-2-acetylaminofluorene (NA-AAF: 1 μM) to measure significant differences in the rates and extents of removal of the induced DNA lesions. Except for mouse cells, removal of covalently bound acetylaminofluorene (AAF) was not as rapid or as extensive as removal of pyrimidine dimers induced by UV light. By 48 hr, only 25%-50% of the NA-AAF damage was removed from the DNA of human cells, whereas 80%-90% of the dimers were removed in 24 hr. Mouse cells appeared to be as competent as human control cells at removing NA-AAF products, but much less efficient at removing dimers. Xeroderma pigmentosum cells (complementation group D) showed much less removal of NA-AAF damage. The data suggest that there may be differences in the pathways by which dimers and certain types of chemical damage are removed. (37 refs.)

77-4266 **Removal of Acetylaminofluorene from the DNA of Control and Repair-deficient Human Fibroblasts.** (Eng.) Amacher, D. E. (Pfizer Medical Res. Labs., Groton, CT 06340) Lieberman, M. W. *Biochem Biophys Res Commun* 74(1): 285-290; 1977.

Control fibroblasts and fibroblasts from patients with Fanconi's anemia and ataxia telangiectasia removed 40%-48% of covalently bound acetylaminofluorene (AAF) from DNA by the end of 24 hr. In contrast, fibroblasts from patients with xeroderma pigmentosum (XP: complementation groups A and C) removed little AAF, while XP variants seemed to remove AAF approx as well as control cells. (19 refs.)

77-4267 **Adduct Formation Between the Carcinogen N-Acetoxy-2-acetylaminofluorene and Synthetic Polydeoxyribonucleotides.** (Eng.) Harvan, D. J. (Natl. Inst. Environmental Health Sciences, NIH, Post Office Box 12233, Research Triangle Park, NC 27709) Hass, J. R.; Lieberman, M. W. *Chem Biol Interact* 17(2): 203-210; 1977.

The chemical carcinogen N-acetoxy-2-acetylaminofluorene was reacted with the alternating DNA polymer, poly(dG-dC)·poly(dG-dC); the homopolymer, poly(dG)·poly(dC); poly(dA-dT)·poly(dA-dT); and poly(dA)·poly(dT). the extent of reaction was greater at lower ionic strengths, but changing the pH of the reaction mixture from pH 8.9 to 5.5 had little effect. The alternating dG/dC polymer was 1.5- to 3-fold more reactive than the dG/dC homopolymer and 10- to 20-fold more reactive than the dA/dT polymers. The major reaction product was 8-(N-2-fluorenylacetamido) deoxyguanosine. The greater reactivity of the alternating dG/dC polymer may be explained by the consequences of local denaturation caused by interaction of the first molecule of carcinogen with a dG moiety. With the homopolymer, subsequent interactions of local dG moieties with carcinogen are restricted by steric factors and base stacking, whereas increased reactivity of dG moieties on both strands is expected with the alternating polymer. (21 refs.)

77-4268 **Role of Sulfotransferase from Rat Liver in the Mutagenicity of N-Hydroxy-2-acetylaminofluorene in *Salmonella typhimurium*.** (Eng.) Mulder, G. J. (Lab. Chemical Pharmacology, Natl. Heart and Lung Inst., NIH, Bethesda, MD 20014) Hinson, J. A.; Nelson, W. L.; Thorgeirsson, S. S. *Biochem Pharmacol* 26(14): 1356-1358; 1977.

The mutagenicity of the sulfate ester of N-hydroxy-2-acetylaminofluorene (N-hydroxy-2-AAF), which has been postulated to be the ultimate carcinogen of 2-AAF and N-hydroxy-2-AAF, was examined in the *Salmonella typhimurium* test system. The mutagenicity test was carried out with strain TA1538 using 3 mg rat liver postmicrosomal fraction/plate. Each plate also contained 1 μg N-hydroxy-2-AAF and, when used, 10 mM p-nitrophenyl sulfate, 20 μM ADP and 0.2 μM p-nitrophenol. N-hydroxy-2-AAF gave rise to relatively few revertants in the absence of the postmicrosomal fraction. In its presence, however, there was a marked increase in the mutagenicity of N-hydroxy-2-AAF. Addition of the sulfation cofactors in the presence of the postmicrosomal fraction and N-hydroxy-2-AAF caused a sharp decrease in mutagenicity. This decrease was largely reversed by p-nitrophenol, which did not decrease the number of revertants when the sulfation cofactors had been omitted. These results indicate that metabolic activation of N-hydroxy-2-AAF by a process other than the one catalyzed by sulfotransferase is more important in mutagenesis in *Salmonella typhimurium* than activation by sulfotransferase. The Salmonella test system may be unable to detect a short-lived, highly reactive, potential mutagen such as the sulfate ester of N-hydroxy-2-AAF because this species arylates other more readily available macromolecules before reaching bacterial DNA· sulfate, 20 μM ADP and 0.2 μM 4p-nitrophenol. N-hydroxy-2-AFF gave rise to relatively few revertants in the absence of the postmicrosomal fraction. In its presence, however, there was a marked increase in the mutagenicity of N-hydroxy-2-AFF. Addition of the sulfation cofactors in the presence of the postmicrosomal fraction and N-hydroxy-2AAF caused a sharp decrease in mutagenicity. This decrease was largely reversed by p-nitrophenol, which did not decrease the number of revertants when the sulfation cofactors had been omitted. These results indicate that metabolic activation of N-hydroxy-2-AAF by a process other than the one catalyzed by sulfotransferase is more important in mutagenesis in *Salmonella typhimurium* than activation by sulfotransferase. The Salmonella test system may be unable to detect a short-lived, highly reactive, potential mutagen such as the sulfate ester of N-hydroxy-2-AAF because this species arylates other more readily available macromolecules before reaching bacterial DNA. (25 refs.)

77-4269 **In Vitro Mutagenic Activation of N-Hydroxy-2-Acetylaminofluorene (N-OH-2-AAF) by Liver Cell Nuclei from Mice and Rats (Meeting Abstract).** (Eng.) Sakai, S. (NIH, Bethesda, MD 20014); Wirth, P. J.; Thorgeirsson, S. S. *Pharmacologist* 19(2): 192; 1977. (no refs.)

77-4270 **Isolation of In Vivo Replicated Rat Metabolite(s) (Meeting Abstract).** (Eng.) Zahner, A. J. (Fels Res. Inst., Temple Univ. Medical Sch., Philadelphia, PA 19140) Rajalakshmi, S.; Sarma, D. S. *Proc Am Assoc Cancer Res* 18: 99; 1977. (no refs.)

77-4271 **Spin Trapping in Biological Systems. Oxidation of the Spin Trap 5,5-Dimethyl-1-pyrroline-1-oxide by a Hydroperoxide-Hematin System.** (Eng.) Floyd, R. A. (Biomembrane Res. Lab., Oklahoma Medical Res. Foundation, Oklahoma City, OK 73104) Soong, L. M. *Biochem Biophys Res Commun* 74(1): 79-84; 1977.

The spin trap 5,5-dimethyl-1-pyrroline-1-oxide was used to determine if primary free radicals are involved in the hematin-cumene hydroperoxide system. This system oxidizes N-hydroxy-2-acetylaminofluorene into its nitroxyl free radical form. The spin trap did not trap free radicals, but was oxidized itself. (11 refs.)

77-4272 **Ascorbate Dependent Conversion of the N-O-Sulfate Ester of 2-Acetylaminofluorene (2AAF) to a Mutagenic Metabolite (Meeting Abstract).** (Eng.) Andrews, L. S. (NIH, Bethesda, MD 20014); Hinson, J. A.; Gillette, J. R. *Pharmacologist* 19(2): 192; 1977. (no refs.)

77-4273 **The Action of a Single Toxic Dose of 2-Acetylaminofluorene or Allylic Alcohol on the Adrenals. II. Effect on Adrenal Cyclic 3′,5′- Adenosine Monophosphate Concentration During the 1st and 2nd Day.** (Eng.) Danz, M. (Pathologisches Institut der Friedrich-Schiller-Universitat, Ziegelmuhlenweg 1, DDR-69 Jena, E. Germany) Kittlick, P. D. *Exp Pathol (Jena)* 13(2-3): 139-144; 1977.

A study was made of the level of cyclic AMP (cAMP) in the adrenals of male Sprague-Dawley rats following a single administration of 150 mg/kg 2-acetylaminofluorene (AAF) or 30 mg/kg allyl alcohol (ALL) by stomach tube. A transient increase in adrenal cAMP levels was seen 10 hr later in both experimental groups relative to controls. At 30-39 hr, ALL intoxication was associated with about a twofold increase in adrenal cAMP concentration, whereas AAF administration was associated with a slight fall in cAMP levels. (47 refs.)

77-4274 **Effects of Hepatic Enzyme Modifiers on the Biotransformation and Binding of 2-Acetylaminofluorene to Tissue Nucleophiles, in Vivo and in Vitro (Meeting Abstract).** (Eng.) Son, O. S. (Coll. Pharmacology, Ohio State Univ., Columbus, OH 43210); Feller, D. R. *Pharmacologist* 19(2): 192; 1977. (no refs.)

77-4275 **Effect of 2-Acetylaminofluorene Ingestion on Hepatic Chromatin Structure (Meeting Abstract).** (Eng.) Schwartz, E. L. (Dept. Pharmacology, Michigan State Univ., East Lansing, MI 48824); Goodman, J. I. *Pharmacologist* 19(2): 181; 1977. (no refs.)

77-4276 **Stimulation of Hepatocellular Proliferation by a Serum Factor from Thioacetamide-treated Rats.** (Eng.) Morley, C. G. (Dept. Biochemistry, Rush Presbyterian-St. Luke's Medical Center, 1753 W. Harrison St., Chicago, IL 60612) Boyer, J. L. *Biochim Biophys Acta* 477(2): 165-176; 1977.

A heat-stable, nondialyzable factor found in the serum of Sprague-Dawley rats treated with thioacetamide for 6-48 hr was able to stimulate hepatic, but not kidney, DNA synthesis in mice and rats; the mitotic index of the livers of treated animals was also increased. The results indicate that thioacetamide-induced liver injury results in the appearance of a humoral factor that stimulates DNA synthesis in rodent liver. This factor has properties similar to a growth-stimulating factor known to occur in the serum of partially hepatectomized rats. (22 refs.)

77-4277 **Hepatocarcinogenesis by Thioacetamide: Correlations of Histological and Biochemical Changes and Possible Role of Cell Injury.** (Eng.) Anghileri, L. J. (Innere Klinik und Poliklinik, Klinikum der Universitat Essen, Hufelandstrasse 55, D-4300 Essen 1, W. Germany) Heidbreder, M.; Weiler, G.; Dermietzel, R. *Exp Cell Biol* 45(1-2): 34-47; 1977.

Male Wistar rats fed a diet containing 0.03% thioacetamide for prolonged periods developed a hepatocarcinogenesis in which morphological changes were associated with important biochemical modifications. An observed calcification of the mitochondria may be significant in the neoplastic transformation of the cell. (22 refs.)

77-4278 **Thalidomide-type Malformations and Subsequent Osteosarcoma (Letter to Editor).** (Eng.) Teppo, L. (Finnish Cancer Registry, 00170 Helsinki 17, Finland) Saxen, E.; Tervo, T.; Partio, E.; von Bonsdorff, H.; Salmela, J.; Avikainen, V.; Isomaki, M.; Krees, R. *Lancet* 2(8034): 405; 1977.

The case history of a mentally and physically retarded boy who developed osteosarcoma at the age of 16 after trauma to the left femur is presented. At birth, the child had malformations of the limbs corresponding to those described in thalidomide cases, and the mother had received many drugs during pregnancy while thalidomide was on the market. (2 refs.)

77-4279 **Mutation Induction by the Antischistosomal Drug F30066 in Various Test Systems.** (Eng.) Ong, T. M. (Natl. Inst. Experimental Health Sciences, Research Triangle Park, NC 27709) Callen, D. F.; Huang, S. L.; Batzinger, R. P.; Bueding, E. *Mutat Res* 48(1): 37-42; 1977.

The genetic activity of furapromidium (F30066), an antischistosomal drug, was studied in *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Neurospora crassa*, and cultured Chinese hamster cells. The compound induced gene mutations in *S. typhimurium*, *N. crassa*, and Chinese hamster cells; it also caused gene conversions in *S. cerevisiae*. Since many mutagenic nitrofurans are also carcinogenic in laboratory animals, F30066 represents a potential carcinogenic hazard to man. (16 refs.)

77-4280 **Carcinogenic Activity of 3-Di(hydroxymethyl)amino -6-(5-nitro-2-furylethenyl)-1,2,4-triazine (Panfuran-S) in Male Rats.** (Eng.) Konishi, Y. (Dept. Oncological Pathology, Cancer Center, Nara Medical Univ., 840 Shiji-cho, Kashihara 634, Japan) Denda, A.; Takahashi, S.; Inui, S.; Kojima, K. *Gann* 68(3): 371-372; 1977.

The carcinogenicity of 3-di(hydroxymethyl)-amino-6-(5-nitro-2- furylethenyl)-1,2,4-triazine (Panfuran-S) was examined in male Wistar rats. Squamous cell carcinomas were found in the stomach and adenocarcinomas were found in the small intestine. This model may be useful for studying adenocarcinoma of the small intestine. (6 refs.)

77-4281 **Studies on the Mutagenicity of Nitrofurans in *Salmonella typhimurium*.** (Eng.) Rosenkranz, H. S. (Dept. Microbiology, New York Medical Coll., Valhalla, NY 10595) *Biochem Pharmacol* 26(9): 896-898; 1977.

Two carcinogenic nitrofurans, N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide (NFTF) and 2-(2,2-dimethylhydrazino)-4-(5-nitro-2-furyl)thiazole (DMNT), were found to be mutagenic in *Escherichia coli* and *Neurospora crassa* and carcinogenic in laboratory animals. However, neither was mutagenic for *Salmonella typhimurium* strains G46, TA1530, TA1535, TA1978, and TA1538 when tested by two modifications of the Ames procedure (spot test and a quantitative agar overlay assay). Because the antibacterial action of these compounds may allow too few survivors to permit the scoring of mutants, a modification of the Ames procedure was used. The bacteria TA1535 and TA1538 were exposed for limited periods (0, 20, 40, 60, and 80 min) to NFTF and DMN in liquid suspension and then processed to determine the number of mutants per survivors, rather than the number of mutants per plate. With this method, the mutagenicity of the two nitrofurans was readily demonstrable. The test agents induced mutations of both the base-substitution and frameshift type. Neither of the two exhibited significant mutagenicity with tester strains deficient in nitroreductase activity. (21 refs.)

77-4282 **Mutagenicity of 3a,8a-Dihydrofuro[2,3-b]benzofuran, a Model of Aflatoxin B_1, for *Salmonella typhimurium* TA100.** (Eng.) Coles, B. F. (Dept. Chemistry Univ. York, Heslington, Yorkshire Y01 5DD, England) Smith, J. R.; Garner, R. C. *Biochem Biophys Res Commun* 76(3): 888-892; 1977.

The 3a,8a-dihydrofuro(2,3-b)benzofuran structure (I) occurs in a number of toxic, mutagenic, and carcinogenic natural products, notably the aflatoxins and sterigmatocystins. It is this function in aflatoxin B_1 (AFB_1) that is metabolically activated to yield the highly reactive epoxide AFB_1-8,9-oxide, which may be responsible for the mutagenic and carcinogenic properties of AFB_1. Compound I has been synthesized chemically and tested for its mutagenicity. In the presence of the 9,000 x g rat liver supernatant fraction, I induced *his*+ revertants in *Salmonella typhimurium* strain TA100 (but not strain TA98), but with only 1/5,000th of the activity of AFB_1. Omission of the rat liver preparation abolished the mutagenicity entirely. It is suggested that one of the following factors may account for the great difference in mutagenicity between I and AFB_1: reduced conversion to epoxide or inability of I to intercalate with DNA. (17 refs.)

77-4283 **Aflatoxins in California Tree Nuts.** (Eng.) Fuller, G. (Western Regional Res. Lab., Agriculture Res. Service, U.S. Dept. Agriculture, Berkeley, CA 94710); Spooncer, W. W.; King, A. D.; Schade, J.; Mackey, B. *J Am Oil Chem Soc* 54: 231A-234A; 1977.

Surveys of the California walnut and almond crops to determine the incidence of aflatoxins showed av proportions of contaminated nuts from the field to be 1 in 28,250 for walnuts and 1 in 26,500 for almonds. The use of electronic and hand sorting for damage was found to be effective in placing contaminated kernels in the inedible rejects. (14 refs.)

77-4284 **Determination of Aflatoxin in Milk and Milk Products.** (Ger.) Polzhofer, K. (Unilever Forschungsgesellschaft mbH, Behringstrasse 154, D-2000 Hamburg 50, W. Germany) *Z Lebensm Unters Forsch* 163(3): 175-177; 1977.

In several milk, milk powder, yoghurt, Camembert, and fresh, hard, and processed cheese samples investigated for possible contents of aflatoxin B_1, B_2, G_1 and M_1, only aflatoxin M_1 was found. Its av and max values were as follows: 0.07 and 0.33 μg/liter (milk), 0.50 and 2.0 μg/kg (milk powder), 0.20 and 0.47 μg/kg (yoghurt), 0.23 and 0.51 μg/kg (fresh cheese), 0.43 and 1.3 μg/kg (hard cheese), 0.26 and 0.55 μg/kg (processed cheese) and 0.31 and 0.73 μg/kg (Camembert). In the winter, the concentration of aflatoxin M_1 in milk was 0.33 μg/liter, compared to a summer value of 0.28 μg/liter. (19 refs.)

77-4285 **Improved Procedure for Quantitative Determination of Aflatoxins in Corn and Wet Milled Corn Products.** (Eng.) Barabolak, R. (Moffett Technical Center, CPC International, Incorporated, Argo, IL 60501) *J Assoc Off Anal Chem* 60(2): 308-310; 1977.

A procedure is described for extracting aflatoxins from a variety of agricultural products with aqueous acetone; ammonium sulfate is used to precipitate extraneous interfering substances in minicolumn screening techniques. (8 refs.)

77-4286 **A Survey of Some Foods for Aflatoxins.** (Eng.) Stanton, D. W. (Chemistry Div., Dept. Scientific and Industrial Res., Auckland, New Zealand). *Food Technol N Z* 12(4): 25; 1977.

A small survey of aflatoxin levels in susceptible, locally available foods in Auckland was conducted. Only two samples of peanuts imported from India showed contamination with aflatoxin B_1 (5 and 6 μg/kg, respectively). (8 refs.)

77-4287 **Reduction of Aflatoxin B1 with Zinc Borohydride: An Efficient Preparation of Aflatoxicol.** (Eng.) Hsia, M. T. (Food Res. Inst., Univ. Wisconsin, Madison, WI 53706); Chu, F. S. *Experientia* 33(9): 1132-1133; 1977.

A procedure is presented for the production of synthetic aflatoxicol by treatment of aflatoxin B1 with ethereal zinc borohydride under essentially neutral conditions. (11 refs.)

77-4288 **Carcinogenic Activity of Petasitenine, a New Pyrrolizidine Alkaloid Isolated from *Petasites japonicus* Maxim.** (Eng.) Hirono, I. (Dept. Pathology, Gifu Univ. Sch. Medicine, Gifu-City 500, Japan) Mori, H.; Yamada, K.; Hirata, Y.; Haga, M.; Tatematsu, H.; Kanie, S. *J Natl Cancer Inst* 58(4): 1155-1157; 1977.

The carcinogenic activity of petasitenine, a new pyrrolizidine alkaloid isolated from the young flower stalk of *Petasites japonicus*, was studied in ACI rats. All three rats that received a 0.05% solution of petasitenine in drinking water died or were killed in moribund condition 72 days after the start of the experiment. They showed necrosis, hemorrhage, and remarkable bile duct proliferation in the liver. In another group that received a 0.01% solution, 8/10 animals surviving > 160 days developed liver tumors, ie, hemangioendothelial sarcoma in 5 rats and liver cell adenomas in 5, 2 of whom simultaneously developed the sarcomas. No tumors were observed in the livers of the control animals. (8 refs.)

77-4289 **Cell Surface Changes Induced by a Single Treatment with Carcinogenic and Noncarcinogenic Agents in Cultures of Newborn Rat Cells.** (Rus.) Belisheva, N. K. (Lab. Tumor Cell Genetics, Inst. Cytology, Acad. Sciences USSR, Leningrad, USSR) Fridliandskaia, I. I. *Tsitologiia* 19(4): 457-459; 1977.

Agglutination of normal rat cells exposed to the carcinogens 7,12-dimethylbenz(a)anthracene (DMBA: 0.1 and 0.05 μg/ml) and dimethylnitrosamine (DMNA: 2,000 μg/ml) and to the DMBA noncarcinogenic analog phenanthrene (0.07 and 0.35 μg/ml) was studied. Both concentrations of DMBA increased the agglutination of the rat cells to levels comparable to those of rat tumor cells from polyaromatic hydrocarbon-induced tumors (no further details). Agglutinability was not affected by DMNA and phenanthrene. (10 refs.)

77-4290 **Somatic Mutagenesis in *D. melanogaster* as a Rapid Method for Testing Carcinogens (N-Nitroso Compounds).** (Rus.) Shabad, L. M. (Scientific Res. Inst. Medical Radiology, Acad. Medical Sciences, USSR, Obninsk, Kaluga Oblast, USSR) Khovanova, E. M.; Logvinenko, E. G.; Belitskii, G. A. *Dokl Akad Nauk SSSR* 231(4): 997-1000; 1976.

The use of induced somatic mosaicism in *Drosophila melanogaster* as a rapid method for testing chemical carcinogens was studied. Virgin females (genotype y+/y+) were crossed with W sn^3/y males in test tubes. The parents were removed after 3 days, and the compounds to be tested (I: N-nitroso-N-methyl-N-nitroguanidine; II: N-nitroso-N-methyl-p-toluenesul- famide; III: N-nitroso-N,N-dimethylamine; IV: N-nitroso-N,N-diethylamine, or V: N-nitroso-N,N-diallylamine) were introduced. The incidence of mosaic spots (yellow, singed, and total number of spots) was determined per 100 larvae. The overall incidences of mosaic spots were 1.05% in the control, 20.2% in the group I, 3.21% in group II, 15.72% in group III, 11.41% in group IV, and 2.20% in group V. The incidence of mosaicism was almost three times as high in females that flew away later than in those that flew away at earlier dates in group IV, which is due to the metabolic activation of the substance in the larvae. Pseudotumors were found in 2-3% of the females that flew away between 4 and 6 days in this group. Compounds I and III caused pseudotumors at very low incidence only, while compounds II and V had no morphogenetic effect at all. Compounds I, III and IV also caused growth retardation. Thus, compounds I, III, and IV proved to be highly active mutagens and morphogens. (13 refs.)

77-4291 **Induction of Lung Tumors in Mice with Diamylnitrosamine.** (Eng.) Zabezhinskii, M. A. (Lab. Chemical Carcinogenic Agents, N. N. Petrov Scientific Res. Inst., Ministry Health USSR, Leningrad, USSR) Balanski, R. M. *Bull Exp Biol Med* 83(1): 83-85; 1977.

Seventeen injections of 0.025 ml diamylnitrosamine give over 23 wk caused lung tumors in CC57W male mice. Th tumors were mainly adenomas, but a few adenocarcinoma were also found. Some animals also developed proliferativ changes in the kidney and urinary bladder. This model coul be useful in the study of pulmonary carcinogenesis. (2 refs.

77-4292 **Hepatocarcinogenic Effect of DENA in Pigs** (Eng.) Graw, J. J. (Central Animals Lab., German Cancer Res. Center, Im Neuenheimer Feld 280, D-690 Heidelberg, W. Germany) Berg, H. *Z Krebsforsch* 89(2) 137-143; 1977.

Diethylnitrosamine (DENA) was fed to five Goettinger minipigs at a dose of 0.4 mg/kg 5x/wk, for a total dose o 420 mg/kg over a 5-yr period. The animals showed multipl neoplasia of the liver with all transitions, including hepatocellular carcinoma and Kupffer cell sarcoma with metastases i the regional lymph nodes and the lung. Two animals ha metastases in the lung as well as one renal carcinoma and on tumor in the hemisphere of the brain. The results demonstrate the organotropic and generalized carcinogenic actio of DENA in the pig. (7 refs.)

77-4293 **The Induction of Tumors in *Rana temporari* with Nitrosamines.** (Eng.) Khudoley, V. V. (Inst. Oncology, USSR Ministry Public Health, 188 646, Leningrad, USSR). *Neoplasma* 24(3): 249-251; 1977.

The use of anurian amphibians in determining the carcinogenicity of nitroso compounds was examined. *Rana temporaria* frogs of both sexes (1-5 yr old) were exposed to dimethylnitrosamine (DMNA, 5 ppm) or diethylnitrosamine (DENA, 50 ppm) dissolved in their tank water. The water solutions were changed six times per week for 29 or 37 wk, respectively. Hepatocellular cancers and adenomas and hemocytoblastosis were induced in 19/43 frogs exposed to DMNA and in 41/94 exposed to DENA. The time of first tumor appearance was 9 wk (DMNA) and 11 wk (DENA). Av tumor latency was 18.2 and 19.7 wk, respectively. The high relative tumor incidence and the short tumor latency suggest the usefulness of amphibians in short-term experiments for the study of nitrosamine tumorigenesis and in assays of environmental pollution by these compounds. These studies may also be important in defining the general and comparative regularities of tumor growth. (11 refs.)

77-4294 **Ultrastructure of N-Dibutylnitrosamine-induced Tumors of the Urinary Bladder in European Hamsters.** (Eng.) Reznik-Schuller, H. (Abteilung fur Experimentelle Pathologie, Medizinische Hochschule Hannover, Karl-Weichert-Allee 9, 3000 Hannover 61, W. Germany); Mohr, U. *J Natl Cancer Inst* 58(5): 1383-1390; 1977.

ectron microscopy was used to investigate the transitional ll and squamous cell carcinomas induced by *N*-utylnitrosamine in European hamsters. The ultrastructure these tumors showed that they are different developmental ges of the same type of tumor rather than two fundamenlly different types of neoplasm. (13 refs.)

-4295 **Mutagenicity of N-Butyl-N-(4-hydroxybutyl) nitrosamine, a Bladder Carcinogen, and elated Compounds.** (Eng.) Nagao, M. (Biochemis- Div., Natl. Cancer Center Res. Inst., Tsukiji 5-1-1, Chuo- , Tokyo 104, Japan) Suzuki, E.; Yasuo, K.; Yahagi, T.; ino, Y.; Sugimura, T.; Okada, M. *Cancer Res* 37(2): 399- 7; 1977.

Butyl-N-(4-hydroxybutyl)nitrosamine (BBN), which setively induces bladder tumors in rats and mice, was mutanic to *Salmonella typhimurium* strains TA1535 and TA100 the presence of an S-9 mix prepared from the liver of rats eated with a polychlorinated biphenyl. NADH was a more fective cofactor than NADPH in the activation of BBN by e rat liver S-9 fraction. N-Butyl-N-(3-rboxypropyl)nitrosamine, reported to be the main urinary etabolite of BBN as well as of N,N-dibutylnitrosamine and own to induce urinary bladder tumors specifically, was utagenic without metabolic activation by the S-9 mix. The utagenicities of 31 compounds related structurally or etabolically to BBN and N,N-dibutylnitrosamine were also sted. Of these compounds, 13 had previously been demonrated to be carcinogenic and 9 had been shown to be noncarnogenic. All the carcinogenic compounds were mutagenic strain TA1535 with or without the S-9 mix. Four of the ne noncarcinogenic compounds were also mutagenic. These alse-positive" compounds were predicted, in fact, to be carnogenic. (27 refs.)

7-4296 **Vascular Changes During Rat Urinary Bladder Carcinogenesis Induced by N-Butyl-N-(4-ydroxybutyl)nitrosamine.** (Eng.) Tatematsu, M. (First ept. Pathology, Nagoya City Univ. Medical Sch., 1 awasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan); ohen, S. M.; Fukushima, S.; Shinohara, Y.; Ito, N. *Gann* 8(1): 127-128; 1977.

he urinary bladder vasculature of male Wistar rats that reeived 0.05% N-butyl-N-(4-hydroxybutyl)nitrosamine in the rinking water was studied electron microscopically each eek for the first 12 wk, then at 40 wk. Results are briefly iscussed. (2 refs.)

7-4297 **Oxidative Biotransformation of Di-n-butylnitrosamine. Formation In Vitro of Aldeydes in the Presence of Rat Liver Microsomes.** (Eng.) Blattmann, L. (Forschergruppe Praventivmedizin, Max-Planck-Institut fur Immunbiologie, D-7800 Freiburg/Breisgau, W. Germany); Preussmann, R. *Z Krebsforsch* 88(3): 311-314; 1977.

The formation of n-butyraldehyde in vitro after incubation of di-n-butylnitrosamine (DBNA) with rat liver microsomes was investigated to obtain evidence of α-C-hydroxylation as a prerequisite in the activation of nitrosamines to form alkylating agents as ultimate carcinogens. DBNA was incubated with a rat liver microsomal fraction in the presence of the necessary NADPH-generating cofactors and oxygen. The reaction products were isolated from the incubation mixture by solvent extraction and separated by thin-layer chromatography, which indicated that butyraldehyde had been formed together with some acetaldehyde and traces of propionaldehyde. These results were confirmed in another experiment using high-resolution mass spectrometry. Formaldehyde was not found. The formation of butyraldehyde from DBNA substantiates the proposed activation mechanism via α-C-hydroxylation. The appearance of acetaldehyde and propionaldehyde indicates that alkyl-chain shortening can occur in nitrosamine metabolism, but its mechanism is not understood. (18 refs.)

77-4298 **Direct Alkyl Chain Cleavage after C-Hydroxylation of Dialkylnitrosamines in Rats. A New Pathway of the Oxidative Biotransformation.** (Eng.) Blattmann, L. (Forschergruppe Praventivmedizin, Max-Planck-Institut fur Immunbiologie, D-7800 Freiburg im Breisgau, W. Germany) *Z Krebsforsch* 88(3): 315-322; 1977.

Comparative in vivo investigations of the biotransformation of di-n-butylnitrosamine (DBNA) and (2-hydroxybutyl)-n-butylnitrosamine (HBBNA) showed the well-known ω-oxidation. However, a new metabolic mechanism of direct oxidative alkyl chain cleavage in the vicinity of the hydroxy group of HBBNA could be demonstrated. Based on the molar excretion ratio of (3-carboxy-2-hydroxypropyl)-n-butylnitrosamine to (carboxymethyl)-n-butylnitrosamine, the relative excretion of the latter metabolite was 6.5 times greater after HBBNA than after DBNA administration. (20 refs.)

77-4299 **Nitrosated Methylcarbamate Insecticides: Effect on the DNA of Human Cells.** (Eng.) Blevins, R. D. (Dept. Health Sciences, E. Tennessee State Univ., Johnson City, TN 37601) Lijinsky, W.; Regan, J. D. *Mutat Res* 44(1): 1-7; 1977.

DNA strand breakage was estimated in normal human skin fibroblasts after treatment with six insecticide esters of N-methylcarbamic acid and with the same insecticides following N-nitroso derivatization: aldicarb (Union Carbide), baygon (Chemagro), BUX-TEN (Chevron), carbofuran (FMC Corp.), landrin (Shell), and methomyl (DuPont). Numerous single-strand breaks were seen in the DNA of all the nitroso derivative-treated cells, but not in the DNA of those treated with the parent insecticides. The effect of the nitroso derivatives on the DNA could be observed for at least 20 hr after removal of the chemical from the cultures. This suggests that the DNA repair events normally occurring in human cells after damage initiated by these agents were not the same as those following UV-type DNA damage or ionizing-type DNA damage in human cells. (10 refs.)

77-4300 **Nitrate, Nitrite, Dimethylnitrosamine and N-Nitrosopyrrolidine in Some Chinese Food Products.** (Eng.) Fong, Y. Y. (Dept. Biochemistry, Univ. Hong Kong, Hong Kong) Chan, W. C. *Food Cosmet Toxicol* 15(2): 143-145; 1977.

Detectable amounts of dimethylnitrosamine (DMNA) and N-nitrosopyrrolidine (NPyr) were found in 27/61 and 23/61 samples of commonly consumed Chinese food products, respectively. There was no correlation between nitrosamine levels and those of nitrate or nitrite. (16 refs.)

77-4301 **Metabolism of the Pancreatic Carcinogen N-Nitroso-2,6-dimethylmorpholine in the Syrian Hamster (Meeting Abstract).** (Eng.) Gingell, R. (Eppley Inst. for Res. in Cancer, Omaha, NB); Nagel, D.; Pour, P. *Toxicol Appl Pharmacol* 41(1): 215; 1977. (no refs.)

77-4302 **Deuterium Isotope Effect in the Activation of Nitrosomorpholine into a Bacterial Mutagen.** (Eng.) Charnley, G. (Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA 02139) Archer, M. C. *Mutat Res* 46(4): 265-268; 1977.

Nitrosomorpholine was found to be five times more mutagenic in *Salmonella typhimurium* TA1535 than nitrosomorpholine-3,3,5,5-d_4. The magnitude of the ratio is consistent with a primary kinetic isotope effect on mutagenicity. Alpha oxidation appears to be involved in the activation process. (11 refs.)

77-4303 **Carcinogenicity of Nitrosoazetidine and Tetradeuteronitrosoazetidine in Sprague-Dawley Rats.** (Eng.) Lijinsky, W. (Chemical Carcinogenesis Program, Frederick Cancer Res. Center, Frederick, MD 21701) Taylor, H. W. *Z Krebsforsch* 89(2): 215-219; 1977.

Nitrosoazetidine was fed to Sprague-Dawley rats in drinking water at three different concentrations. At 2 mM (850 mg total dose), all 15 rats died with hepatocellular carcinomas by the 62nd wk. This was a greater response than that to an equivalent dose of nitrosopyrrolidine. At 0.67 mM, 6/21 rats developed liver tumors, and at 0.17 mM, 2/30 animals had liver tumors. The comparable responses to feeding of nitrosoazetidine-2,4,4-d_4 were 3/21 rats with liver tumors at 0.69 mM and 3/30 rats with liver tumors at 0.17. These results show only a small deuterium isotope effect in liver carcinogenesis with nitrosoazetidine. (8 refs.)

77-4304 **Change of Toxicity and Carcinogenicity of N-Methyl-N-nitrosobenzylamine in Rats by Methyl Substitution in the Phenyl Residue.** (Ger.) Schweinsberg, F. (Hygiene-Institut der Universitat, Silcherstrasse 7, D-7400 Tubingen, W. Germany) Schott-Kollat, P.; Burkle, G. *Z Krebsforsch* 88(3): 231-236; 1977.

Substitution with a methyl group in the 2-, 3-, or 4-position, respectively, of the phenyl moiety of N-methyl-N-nitrosobenzylamine (MNBA) results in a considerable reduction of the acute toxicity (LD50 of MNBA 18 mg/kg, 2-Me-MNBA 90 mg/kg, 3-Me-MNBA 600 mg/kg, and 4-Me-MNBA 400 mg/kg). However, introduction of the methyl groups influences the carcinogenicity of MNBA in rats and its organotrophy only to a small extent. Long-term administration of 5 and 15 ppm, respectively, of the isomeric N-nitroso compounds in the drinking water produces carcinomas of the esophagus and pharynx in all animals. (3 refs.)

77-4305 **Inhibition of the Embryotoxic and Teratogenic Effects of Methylurea and Sodium Nitrite by Various Substances.** (Eng.) Aleksandrov, V. A. (Lab. Experimental Tumors, N. N. Petrov Scientific-Res. Inst. Oncology, Ministry Health USSR, Leningrad, USSR); Dzhioev, F. K. *Bull Exp Biol Med* 83(1): 88-90; 1977.

Intragastric administration of methylurea (30 mg/kg) concurrently with sodium nitrate (50 mg/kg) to noninbred albino rats on the ninth day of pregnancy resulted in 46% fetal mortality. Deformities in the surviving fetuses included hydrocephalus, exencephalus, and herniated liver. (15 refs.)

77-4306 **Individual Susceptibility of Mice to a Mutagen in Both Germ and Somatic Cells.** (Eng.) Aeschbacher, H. U. (Nestle Products Technical Assistance Co. Ltd., Biological Lab., CH-1350 Orbe, Switzerland); Gottwick, D.; Wurzner, H. P. *Mutat Res* 43(1): 71-79; 1977.

A dose-dependent mutagenic effect in both the dominant-lethal and the micro-nucleus tests was observed when male Swiss mice were treated with varying doses of methylurea and sodium nitrite. Susceptibility to mutagenesis differed, but this variation did not appear to be dependent on the liver microsomal metabolizing system. (10 refs.)

77-4307 **Induction of Malformations by N-Methyl-N-nitrosourea (MNU).** (Ger.) Warzok, R. (Pathologisches Institut der Medizinischen Akademie Erfurt, DDR-50 Erfurt, Nordhauser Strasse 74, E. Germany) Thust, R.; Schneider, J.; Rupprecht, E.; Rupprecht, U. *Exp Pathol (Jena)* 13(1): 11-19; 1977.

Multiple malformations observed in a stillborn infant were attributed to maternal inhalation of N-methyl-N-nitrosourea (MNU) or diazomethane. In an attempt to reproduce the same conditions experimentally, 46 pregnant rats were divided into groups and exposed to an atomized solution of 50 mg MNU, to 10.8-32.4 ml diazomethane produced by adding NaOH to MNU, or to 5.0-10.0 mg/kg MNU administered ip or iv. The rats were killed on the 21st day of pregnancy. Malformations that affected the skeleton and CNS were found only in fetuses of rats exposed to iv or ip MNU. External inspection revealed microcephaly, micrognathia, cleft palate, micromelia, syn- and polydactylia, lordosis, and skoliosis of the spinal column as well as deviations of the extremities. In addition, malformations of the skull, hypoplasia, and deviations of the clavicula, scapula, ribs, and bones of the extremities were demonstrated by alizarin red S staining. Complex malformations in the CNS included microencephaly, hydrocephalus, and defects of the septum pellucidum and the corpus callosum. The frequency and spectrum of malformations depended on the dosage and the day of gestation. Diazomethane did not cause malformations, but it did result in a significant increase in dead fetuses. Neither malformations nor toxic effects were observed after inhalation of the atomized MNU solution. The results do not support the hypothesis that the anomalies in the stillborn infant were caused by the mother's contact with MNU. (11 refs.)

77-4308 **The Influence of Prednisolute on the Induction of Neurogenic Tumors in Rats by N-Methyl-N-nitrosourea.** (Eng.) Batka, H. (Institut fur Allgemeine Pathologie und Pathologische Anatomie, Medizinische Akademia, Nordhauser Strasse 74, DDR-50 Erfurt, E. Germany) Warzok, R.; Scholtze, P. *Zentralbl Allg Pathol* 121(1/2): 76-81; 1977.

Repeated ip injections of methylnitrosourea (MNU: 10 mg/kg) led to tumors of the nervous system in 32/44 hooded rats and to extraneural tumors in 38. Combinations of MNU with im injections of the corticosteroid hormone Prednisolute (PS: 0.56 mg/kg) in 42 rats reduced the tumor incidence to 11 for the nervous system and to 17 for extraneural tumors. Of 15 animals that received PS alone, only 1 developed a tumor. The number of animals with multiple tumors was reduced from 34 with MNU alone to 8 with MNU + PS. The av latent period of the first tumor appearance was prolonged from 214 to 289 days. The results show that PS reduces the carcinogenic effect of MNU. In other experiments on the influence of corticosteroids and various carcinogens, ambiguous results were obtained. Although some combinations had results similar to the ones presented, in some combinations the effect of the carcinogen was enhanced by the corticosteroid. (20 refs.)

77-4309 **Interaction of BCNU and X-ray in the Production of DNA Strand Breaks: Differential Response of Normal and Transformed Human Fibroblasts (Meeting Abstract).** (Eng.) Erickson, L. C. (Lab. Molecular Pharmacology, Div. Cancer Treatment, NCI, NIH, Bethesda, MD 20014) *Proc Am Assoc Cancer Res* 18: 64; 1977. (1 ref.)

77-4310 **Effect of Age, Sex, and Intestinal Flora on the Induction of Colon Tumors in Rats.** (Eng.) Balish, E. (Dept. Surgery, Univ. Wisconsin Center Health Sciences and Medical Sch., 1300 University Ave., Madison, WI 53706) Shih, C. N.; Croft, W. A.; Pamukcu, A. M.; Lower, G.; Bryan, G. T.; Yale, C. E. *J Natl Cancer Inst* 58(4): 1103-1106; 1977.

Germ-free and conventional Sprague-Dawley rats were assessed for their susceptibility to intrarectally injected N-methyl-N′-nitrosoguanidine (MNNG) or N-methyl-N-nitrosourea (MNU). The injection dose was 1 mg of carcinogen in 0.2 ml of phosphate buffer. Adenocarcinoma of the colon was induced in germ-free and conventional rats by both MNNG and MNU. The colons of germ-free rats were more susceptible to the direct-acting carcinogens, as manifested by earlier morbidity and development of colon tumors (50% tumors within 30-35 wk), than were those of conventional rats (50% colon tumors within 48-50 wk). Germ-free and conventional male rats were more susceptible to the carcinogens than were their female counterparts. Young (30-day-old) germ-free rats developed colon tumors more quickly (15-20 wk) than did older (60 days) germ-free rats after intrarectal injections of MNNG. No colon tumors were observed in germ-free rats after intrarectal injections of MNN. No colon tumors were observed in germ-free and conventional rats after 72 weekly intrarectal injections with a buffer. Transplantation of an adenocarcinoma induced by MNU in a female rat to germ-free and conventional rats showed that it was easily transplantable, required no immunosuppression, and had essentially the same morphologic characteristics as did the primary tumor. (16 refs.)

77-4311 **Inhibition by L-Ascorbate of Bacterial Mutagenesis Induced by Two N-Nitroso Compounds.** (Eng.) Guttenplan, J. B. (New York Univ. Dental Center, New York, NY 10010) *Nature* 268(5618): 368-370; 1977.

A study was made of the effects of L-ascorbate, which at physiological pH possesses substantial nucleophilicity, on the mutagenesis of *Salmonella typhimurium* strain TA1530 by the alkylating carcinogens N-methyl-N-nitrosoguanidine (MNNG) and dimethylnitrosamine (DMN). Ascorbate was an effective inhibitor of MNNG and DMN mutagenesis, and it was more effective than other physiological nucleophiles. The numbers of revertant colonies caused by MNNG mutagenesis were 3.0 (x $10^3/10^8$ survivors) without any addition, and 0.04, 0.69, 3.3, 2.5, 0.43, 0.62, and 0.54 (x $10^3/10^8$ survivors) with the addition of 0.12 mg/ml of ascorbic acid, creatine, cysteine, methionine, serine, tyrosine, and tryptophan, respectively. The possible mechanism of inhibition of mutagenesis by ascorbate are discussed. The concentration of ascorbate necessary to inhibit mutagenesis by MNNG effectively can readily be exceeded in urine and may be reached in certain tissues. (19 refs.)

77-4312 **Mutagenesis at the Ouabain-resistance Locus in Human Diploid Fibroblasts.** (Eng.) Buchwald, M. (Res. Inst., Hosp. Sick Children, Toronto, Ontario M5G 1X8, Canada) *Mutat Res* 44(3): 401-411; 1977.

Treatment of HSC 172 cells with ethyl methanesulfonate, N-methyl-N′-nitro-N-nitrosoguanidine, and UV light increased the frequency of ouabain resistant mutants in these cells. The conditions for optimum recovery are outlined. This system could be useful in screening for chemical mutagens. (34 refs.)

77-4313 **Carcinogen-Induced Immunoreactivity to Antinucleoside Antibodies in HeLa Cells.** (Eng.) Bases, R. (David and Libbie Coleman Radiology Res. Unit, Dept. Radiology, Albert Einstein Coll. Medicine, Yeshiva Univ., Bronx, NY 10461) Mendez, F.; Neubort, S.; Liebeskind, D.; Hsu, K. C. *Exp Cell Res* 103(1): 175-181; 1976.

Immunoreactivity and ultracentrifugation methods were used to detect carcinogen-induced DNA damage. HeLa cells were exposed to 0-4 μg/ml *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine (MNNG). After exposure to 4 μg/ml MNNG, intense immunoreactivity was observed. Dissociation of the DNA complex was seen at concentrations as low as 0.3 μg/ml MNNG. The results of dose response studies showed that the percentage of immunofluorescent cells increased as the dose of MNNG increased, with the number of immunofluorescent cells approaching 100% at a concentration of 4 μg/ml MNNG. The frequency of DNA strand breaks, as judged by dissociation of the complex and the lowering of the relative moment, was also increased with increasing doses of carcinogen. MNNG and *N*-acetoxy-2-acetylaminofluorene (NAcAAF) were both found to be potent inhibitors of protein synthesis. NAcAAF (10 μg/ml) inhibited protein synthesis by 79%. This concentration of NAcAAF also induced immunoreactivity and dissociated the DNA complex. The effects of MNNG on the immunoreac-
tivity response, on dissociation of the complex, and on pro
synthesis were irreversible. It is possible to detect the act
of chemical carcinogens in animal cells by testing their
munoreactivity to antinucleoside antibodies. This metho
detection was both sensitive and dose dependent. (23 re

77-4314 **Developmental Decline in DNA Repair in N
ral Retina Cells of Chick Embryos: Persist
Deficiency of Repair Competence in a Cell Line Deri
From Late Embryos.** (Eng.) Karran, P. (Dept. Microbiolo
Univ. Chicago, Chicago, IL 60637) Moscona, A.; Strauss.
J Cell Biol 74(1): 274-286; 1977.

The ability of neural retina cells from chick embryos to
form replicative DNA synthesis and DNA excision re
was investigated. It was found that neural retinas of 6-day-
embryos synthesize DNA and are able to carry out D
excision repair. However, in contrast to the situation in
man cells, the max rate of repair induced by N-acet
acetylaminofluorene (AAAF) is no greater than that indu
by methyl methanesulfonate (MMS). With advancing
ferentiation of the retina in the embryo, cell multiplicat
and DNA synthesis decline and cease and, concurrently,
cells lose their ability to carry out DNA excision repair. Th
in 15- to 16-day embryos, in which the level of DNA synt
sis is very low, DNA repair is barely detectable. If reti
from 14-day embryos are dissociated with trypsin and the
suspension is plated in a growth-promoting medium, D
synthesis is reinitiated. However, in these cultures there is
detectable repair of MMS-induced damage, and only low
els of repair are observed after treatment with AAAF. A
line was produced, by repeated passaging of these cultu
in which the cell population reached a steady state of D
replication. However, the cell population remained defici
in its ability to repair MMS-induced damage. This cell
most likely comprises mostly cells of retinoglial origin. Pos
ble correlations between deficiency of DNA repair in replic
ing cells and carcinogenesis in neural tissues are discuss
(30 refs.)

77-4315 **Repair of DNA Damage Induced by Methyl
ing Agents in Human Uterine Cervical Ce
With or Without Cancer Precursor Lesions.** (Eng.) Chau
huri, S. (Medical Div., Smithsonian Science Information
change, 1730 M St., N.W., Washington, DC 20036) Sarn
D. S. *Chem Biol Interact* 17(2): 211-222; 1977.

The capabilities of several human cell lines to repair D
damage caused in vitro by exposure to methylnitrosou
(MNU) or methyl methanesulfonate (MMS) were det
mined. These lines were T_{30}-11 and T_{31}-8 fibroblasts deriv
from normal human uterine cervix, T_4-3F and T_2
fibroblasts derived from cervical dysplasia tissue, T_{19}-
and T_{23}-3 fibroblasts derived from carcinoma *in s*
tissue, T_{12} and T_{18} fibroblasts derived from invas

ırcinoma tissue, GM105 fibroblasts derived from norıal human skin, and T_4-3E epitheliallike cells derived om uterine cervical dysplasia. GM105 and T_4-3E ells repaired 38% and 18%, respectively, of MNUıduced damage in 72 hr, but none of the fibroblast nes from normal uterine cervix (T_{30}-11) or from cervical ells of cancer precursor lesions or neoplastic tissues (T_4-3F, $_{23}$-3, T_{18}) exhibited any significant repair as determined ırough sedimentation profiles in alkaline sucrose gradient f DNA. GM105 cells repaired 40% of MMS-induced DNA amage in 72 hr; T_{30}-11 cells repaired only 16% of this damge in the same period of time. It is concluded that fibroblasts erived from either normal human uterine cervix or from ervix with cancer precursor or cancer lesions exhibit only ow levels of repair of DNA damaged by methylating agents. 32 refs.)

7-4316 **Caffeine Toxicity in Drosophila Strains Having Different MMS Sensitivities.** (Eng.) Nigsch, J. Dept. Zoology, Swiss Federal Inst. Technology, Zurich, Switzerland); Graf, U.; Wurgler, F. E. *Mutat Res* 43(1): 57-3; 1977.

The larvae of four genetically different strains of *Drosophila melanogaster* with different sensitivities to methyl methanesulfonate (MMS) were tested with two caffeine doses. The trains differed significantly in their caffeine sensitivity, but no correlation was found between MMS and caffeine sensitivity. (27 refs.)

77-4317 **The Genetic Conditions in Heterozygous and Homozygous Populations of Drosophila III. EMS Induced Lethal Mutations in Homo- and Heterozygous Populations of *Drosophila melanogaster*.** (Eng.) Karlik, A. (Inst. General Biology, Univ. Vienna, Schwarzspanierstrasse 17, A-1090 Vienna IX, Austria) Feuerbach-Mravlag, H. *Genetica* 47(2): 87-92; 1977.

Several generations of *Drosophila melanogaster*, either monochromosomal or polychromosomal and initially lethal-free, were treated with ethyl methanesulfonate (EMS). The general tendency for the accumulation of recessive lethals was higher in mono- than in polychromosomal populations. Allelism tests showed a high rate of identical lethals in both populations. Therefore, some of the induced lethals seem to be heterotic. (4 refs.)

77-4318 **Acute Lethality of D- and L-Ethionine in Swiss Mice.** (Eng.) Friedman, M. A. (Medical Coll. Virginia, Dept. Pharmacology, Box 726, Richmond, VA 23298) Berry, D. E.; Elzay, R. P. *Cancer Lett* 3(1/2): 71-76; 1977.

The acute lethality of ethionine stereoisomers was investigated in male Swiss mice. The acute, 7-day LD_{50} of D-ethionine administered to the mice ip was determined as 185 mg/kg, with 95% confidence limits of 163 and 210 mg/kg. L-ethionine, the stereoisomer that is more potent in inhibiting liver RNA synthesis, was not lethal at 2,500 mg/kg. This acute toxicity of D-ethionine was suppressed by L-methionine and adenine. Blood accumulation in the thoracic cavity and pericardium was the probable cause of death. (7 refs.)

77-4319 **The Effect of β-propiolactone, Chloromethyl Methyl Ether, and Ethionine on Hepatic Guanylate Cyclase.** (Eng.) Vesely, D. L. (Div. Endocrinology and Metabolism, Dept. Medicine, Univ. Miami Sch. Medicine, Miami, FL 33152) Levey, G. S. *IRCS Med Sci: Cancer* 5(8): 365; 1977.

Treatment of Wistar rat liver, stomach, colon, pancreas, kidney, lung and bladder tissue with β-propiolactone and chloromethyl methyl ether decreased guanylate cyclase activity. Ethionine had no enzymatic effect and N-methyl-N′-nitro-N-nitrosoguanidine stimulated the enzyme. It is suggested that fluctuations in this enzyme level may be involved in mutagenesis. (8 refs.)

77-4320 **Mutagenesis in S49 Mouse Lymphoma Cells: Induction of Resistance to Ouabain, 6-Thioguanine, and Dibutyryl Cyclic AMP.** (Eng.) Friedrich, U. (Dept. Medicine, Div. Clinical Pharmacology, Univ. California at San Francisco, San Francisco, CA 94143) Coffino, P. *Proc Natl Acad Sci USA* 74(2): 679-683; 1977.

The effect of mutagens on resistance to ouabain, 6-thioguanine, and dibutyryl cyclic AMP (Bt_2cAMP) were investigated in mouse S49 lymphoma cells. N-Methyl-N′-nitro-N-nitrosoguanidine (MNNG), ethyl methanesulfonate, ICR 191, and x-rays were used. Ouabain resistance was induced by MNNG, but not by ICR 191. ICR 191 induced resistance to 6-thioguanine more efficiently than did MNNG; the converse was true of resistance to Bt_2cAMP. The relative frequency of biochemically distinguishable subtypes of mutants resistant to Bt_2cAMP was characteristic of the mutagen used to generate them. The results imply that MNNG and ethyl methanesulfonate, but not ICR 191 and x-rays, frequently give rise to DNA base sequence changes that result in structurally altered but functional proteins. This type of change is required for induction of mutants resistant to ouabain and of certain classes of mutants resistant to Bt_2cAMP. Resistance to 6-thioguanine and other classes of mutants resistant to Bt_2cAMP can result from DNA base sequence changes that lead to extensive alteration of protein structure or expression; these changes are induced by ICR 191 or x-rays. (27 refs.)

77-4321 **Chemical Mutation in Human Lymphoblasts.** (Eng.) Thilly, W. G. (Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA 02139) *J Toxicol Environ Health* 2(6): 1343-1352; 1977.

A description is presented of a quantitative assay developed for measuring mutation induced at the *hgprt* locus (gene locus coding for hypoxanthine-guanine phosphoribosyltransferase) in human lymphoblasts. When cell line MIT-2 lymphoblasts derived from a female patient with mononucleosis were treated for 24 hr with 0.5 μg/ml of the substituted acridine ICR-191, the max 6-thioguanine (6TG)-resistant mutant fraction was achieved by day 14 (or 14 continuous generations). 6TG resistance was absolutely linked to deficiency in HGPRT activity. Additional studies of phenotypic lag following treatment of cultures with methylnitrosourea (MNU), methylnitronitrosoguanidine (MNNG), and bromodeoxyuridine (BUdR) achieved similar results. Results regarding the concentration dependence of toxicity and mutagenicity for MNU, MNNG, BUdR, and ICR-191 are summarized. Further use of this assay for predicting human health hazards is discussed. (18 refs.)

77-4322 **Comparative Mutagenicity of ICR-191 to *S. typhimurium* and Diploid Human Lymphoblasts.** (Eng.) Deluca, J. G. (Toxicology Group, Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA) Kaden, D. A.; Krolewski, J.; Skopek, T. R.; Thilly, W. G. *Mutat Res* 46(1): 11-18; 1977.

The concentration-dependent mutagenicity of the half mustard-substituted acridine ICR-191 was measured in *Salmonella typhimurium* strain TA98 and in a diploid human cell line. In both cell systems, approx equigenerational exposure produced mutation linearly related to concentration in the lower range of ICR-191 concentrations tested. Saturation behavior was observed in the human cell assay but not in the bacterial assay. However, a 25-fold greater concentration of ICR-191 was required to induce a significant rise in the mutant fraction in the *S. typhimurium* assay than in the human cell assay (6.25 μM vs 0.25 μM). These differences may be linked to differences in the biochemical events required for mutation or in the time of exposure to ICR-191. (16 refs.)

77-4323 **Failure of the Acridine Mustard ICR 191 to Induce DNA Repair in Haploid Frog and Diploid Human Fibroblast Cultures (Meeting Abstract).** (Eng.) Viceps-Madore, D. (Inst. Cancer Res., Fox Chase Cancer Center, Philadelphia, PA 19111) Mezger-Freed, L. *Proc Am Assoc Cancer Res* 18: 105; 1977. (no refs.)

77-4324 **Effect of Acridine Orange on the Recovery from the Injury Induced by Alkylating Chemicals and Gamma Rays in Rice Seeds.** (Eng.) Soomro, A. M. (Atomic Energy Agricultural Res. Centre, Tandojam, Pakistan); Yamaguchi, H. *Radioisotopes* 26(1): 38-41; 1977.

Treatment of rice seeds with acridine orange (AO) either immediately or 48 hr after gamma-irradiation resulted in enhancement of radiation damage to the seedlings. AO post-treatment also potentiated ethylmethane sulfonate and diethyl sulfate damage on seedling height when carried out 24 hr after recovery from these agents. AO potentiated methyl nitrosourea damage 48 to 72 hr after treatment. (15 refs.)

77-4325 **Effects of Treating Drosophila Females with TEM on Their Mortality, and the Yields of Mutation Recovered from X-irradiated Sperm.** (Eng.) Mollet, P. (Dept. Radiation Genetics and Chemical Mutagenesis, Univ. Leiden, Leiden, The Netherlands). *Mutat Res* 43(1): 65-70; 1977.

When ring-x-bearing Drosophila males were x-irradiated and mated to females that had been injected with triethylenemelamine (TEM), the mortality of the females was slightly increased; but the yield of mutations recovered from the irradiated spermatozoa was not influenced. (11 refs.)

77-4326 **Phototype Herpes Therapy--Cassandra Confirmed?** (Eng.) Berger, R. S. (501 George St., New Brunswick, NJ 08903) Papa, C. M. *JAMA* 238(2): 133-134; 1977.

Three recent cases of multiple lesions of the penis (Bowen's disease) following phototype therapy for herpes progenitalis are cited as a further reason for discontinuing the use of this procedure in clinical practice. (12 refs.)

77-4327 **Frameshift Mutagenesis in Bacteria by 8-Methoxypsoralen (Methoxalen) in the Dark.** (Eng.) Bridges, B. A. (M.R.C. Cell Mutation Unit, Univ. Sussex, Falmer, Brighton BN1 9QG, England) Mottershead, R. P. *Mutat Res* 44(3): 305-312; 1977.

Frameshift mutations were induced in *Escherichia coli* and *Salmonella typhimurium* by 8-methoxypsoralen (8-MOP) under dark conditions. The chemical works in a noncovalent manner during DNA replication. The possibility of genetic risk to man resulting from treatment of psoriasis with 8-MOP cannot be excluded. (14 refs.)

77-4328 **Reaction of DNA with Glycidaldehyde. Isolation and Identification of a Deoxyguanosine Reaction Product.** (Eng.) van Duuren, B. L. (Lab. Organic hemistry and Carcinogenesis, Inst. Environmental Medi-ine, New York Univ. Medical Center, New York, NY 0016) Loewengart, G. *J Biol Chem* 252(15): 5370-5371; 977.

he reaction of glycidaldehyde with calf thymus DNA result-d in fusion of a Δ^4-imidazoline ring to the pyrimidine ing of deoxyguanosine. It is suggested that this might e the mode of action for this carcinogen. (13 refs.)

7-4329 **Kaposi's Sarcoma after Long-Term Alkylating Agent Therapy for Multiple Myeloma.** (Eng.) apadia, S. B. (Dept. Pathology, Univ. Pittsburgh Sch. Medicine, Pittsburgh, PA) Krause, J. R. *South Med J* 70(8): 011-1013; 1977.

70-yr-old man developed Kaposi's sarcoma after 3 yr of nelphalan and prednisone treatment for multiple myeloma. t is suggested that immune suppression may allow a clone f malignant cells to emerge and multiply. (13 refs.)

77-4330 **Acute Leukemia After Alkylating-Agent Therapy of Ovarian Cancer.** (Eng.) Reimer, R. R. (Environmental Epidemiology Branch, Landow Building, Room A521, NCI, Bethesda, MD 20014) Hoover, R.; Fraumeni, J. F.; Young, R. C. *N Engl J Med* 297(4): 177-181; 1977.

The leukemogenic potential of alkylating agents used in treating ovarian cancer was evaluated using both a historical and a current survey of cancer patients. A survey of 13,309 patients with ovarian cancer in the National Cancer Institute's End Results Program (1935-1971) indicated no inherent risk of leukemia in patients with this tumor. In contrast, 13 cases of acute nonlymphocytic leukemia occurred among 5,455 patients with ovarian cancer treated at 70 institutions from 1970 through 1975 (compared to 0.62 case expected). All 13 had received treatment with alkylating agents and 9 had also received radiation therapy. The relative risk for patients receiving chemotherapy was 36.1; for patients followed for at least 2 yr, this risk increased to 171.4. Alkylating agents appear to be implicated in these cases of leukemia, and their effect may be enhanced by radiation exposure. (40 refs.)

77-4331 **Development of Chronic Granulocytic Leukemia in a Patient Treated with Pyrimethamine.** (Eng.) Jim, R. T. (Univ. Hawaii Sch. Medicine, Honolulu, HI) Elizaga, F. V. *Hawaii Med J* 36(6): 173, 176; 1977.

The case history of a 51-yr-old woman who developed chronic granulocytic leukemia after treatment with pyrimethamine, sulfisoxasole and prednisone is presented. Either the pyrimethamine or the combination of the three drugs may have had an oncogenic effect. (1 ref.)

77-4332 **Lethal Mutations Due to the Isomeric Forms of the Antileukemic Drug Dimethylmyleran.** (Eng.) Hemsworth, B. N. (Life Science Lab., Teesside Polytechnic, Middlesbrough, Cleveland, England) Wardhaugh, A. A. *IRCS Med Sci: Cancer* 5(7): 341; 1977.

Studies with fertile, Swiss albino mice fed a diet containing isomers of dimethylmyleran indicated that dominant lethal mutations were induced during spermatogenesis. The value of these isomers in chemotherapy remains to be assessed. (6 refs.)

77-4333 **Mammalian Host- and Fluid-mediated Mutagenicity Assays of Captan and Streptozotocin in *Salmonella typhimurium*.** (Eng.) Ficsor, G. (Dept. Biology, Western Michigan Univ., Kalamazoo, MI) Bordas, S.; Wade, S. M.; Muthiani, E.; Wertz, G. F.; Zimmer, D. M. *Mutat Res* 48(1): 1-16; 1977.

The mutagenicity of captan and streptozotocin (SZN) was tested in vivo by reversion of *hisG46* base-pair substitution auxotrophs of *Salmonella typhimurium* in the peritoneal cavity or in the blood, plasma, or urine of Sprague-Dawley rats and Swiss albino mice. In a host-mediated assay of mutation frequency in mice with the *hisG46* mutant, captan gave negative results after three 500-mg/kg doses sc or a 1,000-mg/kg dose po; a 2,000-mg/kg dose po was not mutagenic in rats with the *hisG46, urvB* (TA1950) mutant. SZN induced many reversions at 0.5 mg/kg ip and at 10 or 100 mg/kg po. Captan in the blood or urine of mice given a 250-mg/kg dose po was not mutagenic in *hisG46*. Similarly, captan in the blood of rats given 1,000 mg/kg ip or 2,000 mg/kg po was not mutagenic in TA1950. SZN gave positive results in both fluids. In a semiquantitative test (number of revertants/plate), the mutagenicity of 1,000 μg/ml captan, but not 5,000 μg/ml, was inactivated by rat or human blood during a 45-min incubation at 37 C. The corresponding values in a quantitative test (revertant frequency) were 500 and 1,000 μg/ml. The inactivation was attributed to RBC glutathione. (34 refs.)

77-4334 **Enhancement of Human Guanylate Cyclase Activity by Chemical Carcinogens.** (Eng.) Vesely, D. L. (Div. Endocrinology and Metabolism, Dept. Medicine, Univ. Miami Sch. Medicine, Miami, FL 33152) Levey, G. S. *Proc Soc Exp Biol Med* 155(3): 301-304; 1977.

The effect of three carcinogens, streptozotocin (S), methylnitrosourea (MNU), and hydrazine (H) on guanylate cyclase (GC) activity in a variety of human tissues was investigated. Normal human tissues were obtained from autopsies performed 1-12 hr after death. Both S (10 mM) and MNU (10 mM) enhanced GC activity two- to sixfold in all tissues tested. The order of potency for stimulation by MNU was colon > liver > breast > kidney > duodenum > lung > stomach > pancreas. These results were similar to those with S, except that the breast was the least sensitive to S. The dose-response relationship of the two agents was similar, supporting the concept that the nitrosourea moiety is responsible for GC activation. At 10 mM, it had no effect. At 100 mM, however, max stimulation resulted that was much higher than that produced by S and MNU, being 52-fold in pancreas, 35-fold in kidney, 21-fold in lung, 24-fold in breast, 9-fold in liver, 7-fold in duodenum, and 3-fold in stomach. GC activity was also determined in three human tumors (squamous cell lung carcinoma, ductal breast carcinoma, pancreatic adenocarcinoma). All three tumors had GC activity that was stimulated significantly by the three agents. In enhancing GC activity, the three carcinogens catalyze the production of cyclic guanosine monophosphate (GMP). Cyclic GMP is involved in several processes related to cell growth, and it has recently been implicated in malignant cell transformation. (27 refs.)

77-4335 **Alkylated Purines in the DNA of Various Rat Tissues after Administration of 1,2-Dimethylhydrazine.** (Eng.) Likhachev, A. J. (N. N. Petrov Res. Inst. Oncology, 68, Leningradskaya St., Posjelok Pesochny-2, Leningrad 188646, USSR); Margison, G. P.; Montesano, R. *Chem Biol Interact* 18(2): 235-240; 1977.

The alkylation products of 1,2-dimethylhydrazine were investigated in various tissues of male BD-VI rats after sc injection of the carcinogen. More O^6-methylguanine was found in the DNA of the colon (the target tissue) than in the DNA of the liver, indicating that the colon has a much lower capacity for O^6-methylguanine excision. (19 refs.)

77-4336 **Influence of High and Low Fibre Diet on Induction of Colorectal Tumours in the Rat Using Dimethylhydrazine HCI (Meeting Abstract).** (Eng.) Carachi, R. (Univ. Dept. Surgery, Royal Infirmary, Glasgow, Scotland); Busuttil, A.; Joffe, S. N. *Gut* 18(5): A410-A411; 1977. (no refs.)

77-4337 **Liver Neoplasms and the Oral Contraceptives.** (Eng.) Keifer, W. S. (1145 Broadway, Seattle, WA 98122); Scott, J. C. *Am J Obstet Gynecol* 128(4): 448-454; 1977.

The relationship between liver neoplasms and oral contraceptives is considered. From 1954, when oral contraceptives were first introduced, to 1970, no cases of liver tumors associated with oral contraceptives were reported. Since 1970, however, 138 cases have been reported in the English literature and an additional 9 cases were identified by reviewing the 1970-1976 records from five major US hospitals. Six of the nine had used oral contraceptives and three had not. A case report is given of a 28-yr-old woman who had been taking mestranol plus ethynodiol diacetate for 11 mo. She presented with absent menses and a sensation of fullness or pressure in the right upper abdomen. Because of a palpable mass, abnormal enzyme studies, and radiographic findings, an exploratory operation was performed. A benign hepatic adenoma was found and removed. Tabulated data from 96 cases reveal that women with liver neoplasms and a history of oral contraceptive use outnumber women with liver neoplasms and no contraceptive by > 2:1. Mestranol was the most frequent estrogen used. The most common progestins used were norethindrone and norethynodrel. Exposure varied from 3 to 132 mo. Carcinoma of the liver occurred in eight contraceptive users. There were 11 deaths in 70 cases for a mortality rate of 16%. Of the 11 deaths, 3 patients had malignancies and 8 had benign lesions. This clinical entity seems to fit into three categories: (1) a group of women with the liver neoplasm presenting as an incidental finding (21%); (2) a group with evidence of intra-abdominal rupture (37%); and (3) a group presenting with various complaints associated with pain and a palpable mass (42%). (44 refs.)

77-4338 **Controlled Study of the Association Between Oral Contraception and Hepatocellular Adenoma (Meeting Abstract).** (Eng.) Rooks, J. (Center for Disease Control, Atlanta, GA 30333); Ory, H.; Ishak, K.; Strauss, L.; Greenspan, J. R. *Am J Epidemiol* 106(3): 233; 1977. (no refs.)

77-4339 **The Association of Specific Oral Contraceptive Compounds and Development of Hepatocellular Adenomas (Meeting Abstract).** (Eng.) Ory, H. W. (Center for Disease Control, Atlanta, GA 30333); Rooks, J. B.; Ishak, K. G.; Greenspan, J. R.; Strauss, L. T.; Tyler, C. W. *Am J Epidemiol* 106(3): 233; 1977. (no refs.)

77-4340 **Oral Contraceptives and Cervical Carcinoma.** (Eng.) Boyce, J. G. (Dept. Obstetrics and Gynecology, State Univ. New York-Downstate Medical Center, 450 Clarkson Ave., Brooklyn, NY 11203) Lu, T.; Nelson, J. H.; Fruchter, R. G. *Am J Obstet Gynecol* 128(7): 761-766; 1977.

In a case-control study, the relationship between oral contraceptives and cervical carcinoma was investigated in 689 consecutive patients. Control patients were matched for age, ethnic origin, age at first pregnancy, age at first coitus, and socioeconomic status. There was no significant difference between case and control subjects in duration of oral contraceptive use, type of estrogen used (ie, mestranol or ethinyl estradiol), or years in which the contraceptives were used. The nean duration of oral contraceptive use was 30.9 mo for the ase subjects and 30.2 mo for the control subjects. (12 refs.)

7-4341 **Is the Replacement Hormone Therapy Associated with Breast Cancer? (Meeting Abstract).** Eng.) Choi, N. W. (Univ. Manitoba, Winnipeg, Manitoba, Canada R3E OW3); Nelson, N. A.; Abu-Zeid, H. A. *Am J Epidemiol* 106(3): 233; 1977. (no refs.)

7-4342 **Serum α-Fetoprotein Concentration in Adult Patients under Corticoid, Estroprogestative or Androgen Therapy.** (Eng.) Chayvialle, J. A. (Inserm, U 45, Hopital Edouard-Herriot, F-69374 Lyon Cedex 2, France); Courpron, P.; Mikaelian, S.; Lambert, R. *Digestion* 15(3): 223-226; 1977.

Radioimmunoassay showed no change in the serum α-fetoprotein level in 25 women taking estrogen and progesterone for 1 mo to 5 yr for contraception, in 11 patients with rheumatoid arthritis given long-term corticosteroids, and in 6 patients under androgen therapy for aplastic anemia. (12 refs.)

77-4343 **Pathologic Changes in Mice Induced by Diethylstilbestrol and 17β-Estradiol (Meeting Abstract).** (Eng.) Highman, B. (Univ. Arkansas Coll. Medicine, Little Rock, AR); Norvell, M. J.; Shellenberger, T. E. *Toxicol Appl Pharmacol* 41(1): 178-179; 1977. (no refs.)

77-4344 **Effect of Prenatal Treatment with Ethinyl Estradiol on the Mouse Uterus and Ovary.** (Eng.) Yasuda, Y. (Dept. Anatomy, Faculty Medicine, Kyoto, Univ., Kyoto Japan) Kihara, T.; Nishimura, H. *Am J Obstet Gynecol* 127(8): 832-836; 1977.

Prenatal administration of oral ethinyl estradiol (0.01 or 0.02 mg/kg) before development of the uterine and ovarian blastemas resulted in cystic glandular hyperplasia with epidermization in the endometrium and excessive formation of degenerating follicles in the ovaries of ICR-JCL mice at 10-14 wk of age. (7 refs.)

77-4345 **Studies on the Influence of Exogenous Estrogens on the Cervical Mucosa of Calves.** (Ger.) Schwarz, R. (Anatomisches Institut, Klinik fur Geburtshilfe und Gynakologie des Rindes der Tierarztlichen, Hochschule Hannover, Bischofsholer Damm 15, D-3000, Hannover 1, W. Germany) Grunert, E.; Sperber, E. *Arch Lebensmittelhyg* 28(2): 41-44; 1977.

Administration of exogenous estrogens to calves caused a folding in the cervical mucous membrane as well as a marked epithelial reaction and change in epithelial thickness. The results of biochemical, chemical and additional morphological investigations confirmed these findings. (15 refs.)

77-4346 Separation of Factors that Inhibit or Stimulate DMBA-Induced Breast Tumors, from Both Fetal and Adult Rat Tissues (Meeting Abstract). (Eng.) Noval, J. J. (Dept. Surgery, Temple Univ. Medical Sch., Philadelphia, PA 19140) Obando, M.; Reichle, R. M.; Ryzlak, M. T.; Reichle, F. A. *Proc Am Assoc Cancer Res* 18: 141; 1977. (2 refs.)

77-4347 **Endometrial Carcinoma Following Estrogen-Progestogen Therapy in Turner's Syndrome. A Case Report and Review of the Literature.** (Eng.) Krishnamurthy, S. (Dept. Lab. Medicine and Pathology, Univ. Minnesota Medical Sch., Minneapolis, MN 55455) Adcock, L. L.; Okagaki, T. *Gynecol Oncol* 5(3): 291-298; 1977.

The case history of a 34-yr-old woman with Turner's syndrome who developed endometrial carcinoma 15 yr after sequential estrogen-progestogen therapy and 3 additional yr of combined therapy is presented. Ten cases from the literature of Turner's syndrome, endometrial carcinoma and long-term hormonal therapy are reviewed. (32 refs.)

77-4348 **Endometrial Response to Estrogen and Progesterone Therapy in Patients with Gonadal Dysgenesis.** (Eng.) Benjamin, I. (14 York Drive, Great Neck, NY 11021) Block, R. E. *Obstet Gynecol* 50(2): 136-138; 1977.

A study was made of 16 patients with gonadal dysgenesis who had received cyclic replacement with conjugated estrogens for 2 to 10 yr and of 9 additional patients who received medroxyprogesterone in addition to the conjugated estrogens for 2 to 5 yr. The results indicate an increased risk of endometrial hyperplasia and neoplasia in these patients. It is not known whether this risk is due to therapy or the dysgenesis. (14 refs.)

77-4349 **The Development of Prostatic Adenocarcinoma in Nb Rats Following Prolonged Sex Hormone Administration.** (Eng.) Noble, R. L. (Dept. Physiology, Univ. British Columbia, Vancouver, British Columbia, Canada) *Cancer Res* 37(6): 1929-1933; 1977.

Adenocarcinomas of the dorsal lobe of the prostate gland were induced in Nb rats by the sc insertion of pellets containing testosterone propionate (TPP). The spontaneous incidence of prostate cancer in Nb rats is very low (0.45%). Of 30 rats implanted with two 10-mg TPP pellets, 5 developed carcinoma of the prostate with a mean development time

(MDT) of 57 wk; 11/55 rats treated with three TPP pellets developed tumors with a MDT of 64 wk. When estrone pellets were inserted with the TPP pellets, the tumor MDT was reduced: 8/45 rats treated with estrone and three pellets of TPP developed tumors with MDT of 43 wk. The tumors tended to metastasize, and they were transplanted readily; all were autonomous, except for one that exhibited the growth pattern of a typical estrogen-dependent tumor. The possibility of a hormonal etiology of prostate cancer in humans should be reconsidered. (21 refs.)

77-4350 **Tumor Formation in Preneoplastic Mammary Nodule Lines in Mice Treated with Nafoxidine, Testosterone, and 2-Bromo-α-ergocryptine.** (Eng.) Medina, D. (Dept. Cell Biology, Baylor Coll. Medicine, Houston, TX 77030) *J Natl Cancer Inst* 58(4): 1107-1110; 1977.

The tumor potentials of five preneoplastic mammary nodule lines were examined in BALB/cCrgl mice treated with either nafoxidine (40 mg sc), an estrogen antagonist; 2-bromo-α-ergocryptine (100 mg sc), a prolactin suppressant; or testosterone (18-mg pellet). The inhibitory effect of any of the three agents depended on the individual nodule line and was not correlated with the effects of ovariectomy. Nafoxidine inhibited tumor formation only in nodule line D2, testosterone inhibited tumor formation in lines C3 and C4, and 2-bromo-α-ergocryptine failed to inhibit tumor formation in any of the nodule lines. These results provided information on the range of responses of mouse preneoplastic mammary tissues to a variety of antihormone treatments and suggest that responses to ovariectomy need not be correlated with responses to specific antihormone treatments. (21 refs.)

77-4351 **Modifications of Pituitary Hormones in Altered Thyroid States and Their Relation to Mammary Tumorigenesis (Meeting Abstract).** (Eng.) Cave, W. T. (Dept. Medicine, Univ. Virginia, Sch. Medicine, Charlottesville, VA 22901) Dunn, J. T.; MacLeod, R. M. *Proc Am Assoc Cancer Res* 18: 136; 1977. (no refs.)

77-4352 **Dimethylbenzanthracene (DMBA) and the Protein Binding of Progesterone (Meeting Abstract).** (Eng) Funder, J. W. (Medical Res. Centre, Prince Henry's Hosp., Melbounre, Australia); Barlow, K. M. *Eur J Clin Invest* 7(3): 220; 1977. (no refs.)

77-4353 **Oestrogen Receptor Activity and Endocrine Status in DMBA-induced Rat Mammary Tumours.** (Eng.) Hawkins, R. A. (Dept. Clinical Surgery, Univ. Edinburgh, Edinburgh, Scotland) Hill, A.; Freedman, B.; Killen, E.; Buchan, P.; Miller, W. R.; Forrest, A. P. *Eur J Cancer* 13(3): 223-228; 1977.

Estrogen receptor activity (unfilled sites) was determined in 7,12-dimethylbenz(a)anthracene-induced mammary tumors of Sprague-Dawley rats. At sacrifice, plasma estradiol-17β and prolactin concentrations were determined by radioimmunoassay. In intact animals, tumor receptor levels fluctuated in inverse relationship to the plasma estrogen concentration; following ovariectomy, tumor estrogen receptor concentrations and the plasma levels of both estradiol-17β and prolactin were significantly reduced. Administration of estradiol-17β (1-5 mg in corn oil, sc) to ovariectomized animals did not affect receptor levels, but administration of perphenazine (5 mg/kg, sc) restored the levels to those seen in intact animals. In animals bearing two or more tumors receptor levels were similar in each tumor. It is concluded that the concentration of estrogen receptor sites in rat mammary tumors is influenced by circulating estrogen and prolactin levels. (29 refs.)

77-4354 **Early Increases in Ribonucleic Acid Polymerase Activities of Dimethylbenzanthracene-induced Mammary Tumour Nuclei in Response to Oestradiol-17β and Tamoxifen.** (Eng.) Nicholson, R. I. (Tenovus Inst. Cancer Res., Welsh Natl. Sch. Medicine, Heath Park, Cardiff, CF4 4XX, Wales) Davies, P.; Griffiths, K. *J Endocrinol* 73(1): 135-142; 1977.

The early effects of iv tamoxifen (100 μg) and estradiol-17β (5 μg) on mammary tumors induced in Sprague-Dawley rats by 7,12-dimethylbenz(a)anthracene (20 mg, by intubation) were compared to clarify the action of tamoxifen in inducing early estrogenlike responses but ultimately causing tumor regression. Both substances caused a depletion of cytoplasmic receptor, a concomitant increase in nuclear receptor, and a subsequent replenishment of cytoplasmic receptor. Tamoxifen and estradiol-17β induced a transient increase in RNA polymerase B activity, followed by increases in RNA polymerase A and, again, RNA polymerase B activity. Tamoxifen, unlike estradiol-17β, could not maintain replenishment of cytoplasmic receptor, the increase in RNA polymerase A activity, or the secondary rise in RNA polymerase B activity. The basic antiestrogenic properties of tamoxifen may be implicit in its inability to maintain estrogenic stimulation, and they may be linked to its retention time within the nuclei. (25 refs.)

77-4355 **Effects of Oestradiol-17β and Tamoxifen on Nuclear Oestradiol-17β Receptors in DMBA-induced Rat Mammary Tumours.** (Eng.) Nicholson, R. I. (Tenovus Inst. Cancer Res., Welsh Natl. Sch. Medicine, Heath, Cardiff, CF4 4XX, Wales) Davies, P.; Griffiths, K. *Eur J Cancer* 13(3): 201-208; 1977.

An exchange assay was developed for the measurement of nuclear estradiol-17β binding sites in 7,12-dimethylbenz(a)anthracene-induced mammary tumors of

Sprague-Dawley rats. The assay was used to examine the nuclear concentration of binding sites following the iv administration of tamoxifen (100 μg) and estradiol-17β (5μg). Both compounds translocated receptor protein to the nucleus and caused an early elevation in cytoplasmic receptor levels. By 24 and 48 hr after tamoxifen administration, the intranuclear concentration of the estrogen receptor complex had returned to pretreatment levels. At this time, replenishment of the cytoplasmic receptor had not occurred and the tumors were nonresponsive to estradiol-17β. (17 refs.)

77-4356 **Chemical Carcinogens Stimulate Canine Kidney (MDCK) Cells to Produce Prostaglandins.** (Eng.) Levine, L. (Dept. Biochemistry, Brandeis Univ., Waltham, MA 02154). *Nature* 268(5619): 447-448; 1977.

Treatment of MDCK canine kidney cells with several carcinogenic aromatic hydrocarbons, aflatoxin B_1 and 1,2,7,8-diepoxyoctane increased prostaglandin production relative to carcinogenicity of the chemical. The MDCK line could prove to be a sensitive indicator for the carcinogenic potential of hydrocarbons. (13 refs.)

77-4357 **Aqueous Extracts of Liver and Spleen of Aged Rats as Inhibitors of Chemically Induced Liver and Mammary Carcinomas.** (Eng.) Caesar, G. (Luther Coll., Univ. Saskatchewan, Regina, Saskatchewan S4S 0A2, Canada) *IRCS Med Sci: Cancer* 5(8): 366; 1977.

Extracts of liver and spleen from Wistar rats who had died of old age (approx 3 yr old) had a protective effect against tumor induction in young rats given N-2-fluorenyldiacetamide or 7,12-dimethylbenz(a)anthracene. (9 refs.)

77-4358 **A Fine Structural Study on the Therapeutic Effects of an Aromatic Retinoid on Chemically-induced Skin Papillomas of the Mouse.** (Eng.) Matter, A. (Pharmaceutical Res. Dept., F. Hoffmann-La Roche and Co., Ltd., Basel, Switzerland) Bollag, W. *Eur J Cancer* 13(8): 831-838; 1977.

Skin papillomas induced in female Swiss albino mice by dimethylbenzanthracene and croton oil were treated systemically with a single injection of an aromatic new retinoid ethyl all-trans-9-(4-methoxy-2,3,6-trimethylphenyl)-3,7-dimethyl-2,4,6,8 -nonatetraenoate (Ro 10-9359). A marked tumor regression occurred within 7 days. The effects of this drug as seen with the electron microscope were (1) marked enhancement of production of mucopolysaccharides and their secretion into the extracellular space, (2) labilization of the plasma membrane resulting in vacuolization and loss of cytoplasmic constituents into the extracellular space, (3) increase in lysosomes, and (4) formation of many necrotic cells. There were no clear-cut effects on either the nuclei, nucleoli, or cytoplasmic constituents such as ribosomes and tonofibrils, nor was there any increase in the number of gap junctions, as seen in keratoacanthomas after local retinoic acid treatment. The results favor the hypothesis that cell necrosis is due mainly to labilization of the plasma membrane, although enhanced mucopolysaccharide secretions into the extracellular space might also play a role in papilloma regression. (23 refs.)

77-4359 **Mutagenicity and Cytotoxicity of Benz(a)anthracene Diol Epoxides and Tetrahydroepoxides: Exceptional Activity of the Bay Region 1,2-Epoxides.** (Eng.) Wood, A. W. (Dept. Biochemistry and Drug Metabolism, Hoffmann-La Roche, Inc., Nutley, NJ 07110) Chang, R. L.; Levin, W.; Lehr, R. E.; Schaefer-Ridder, M.; Karle, J. M.; Jerina, D. M.; Conney, A. H. *Proc Natl Acad Sci USA* 74(7): 2746-2750; 1977.

Several diol epoxides and tetrahydroepoxides of benz(a)anthracene (BA) were synthesized and evaluated for mutagenic activity in strain TA100 *Salmonella typhimurium* and in line V79-6 Chinese hamster lung cells. The two diastereomeric 1,2-epoxides of the trans-3,4-dihydrodiol of BA were 15-35 times more mutagenic to the bacteria and 65-125 times more mutagenic to the mammalian cells than were the diastereomeric pairs of BA-8,9-diol-10,11-epoxides or BA-10,11-diol-8,9-epoxides. 1,2-Epoxy-1,2,3,4-tetrahydro-BA was the most mutagenic and cytotoxic of the nine derivatives and was 5 and 25 times more mutagenic than 3,4-epoxy-1,2,3,4-tetrahydro-BA in bacterial and mammalian cells, respectively. In either test system, BA 5,6-oxide (K-region oxide) had $<$ 10% of the activity of any of the 1,2-epoxides derived from BA. The relative stabilities of the derivatives in aqueous solution cannot account for the differences in mutagenicity, because the more mutagenic derivatives tended to be less stable. As had been found for the benzo(a)pyrene diol epoxides, the diol epoxides of BA were also very poor substrates for purified epoxide hydrase. The exceptional mutagenic activity of the 1,2-epoxide derivatives of BA is consistent with and supports the hypothesis that bay region epoxides on saturated, angular benzo rings of unsubstituted polycyclic aromatic hydrocarbons are ultimate carcinogens. (34 refs.)

77-4360 **The Metabolic Activation of 7-Methylbenz(a)anthracene in Mouse Skin.** (Eng.) Tierney, B. (Chester Beatty Res. Inst., Inst. Cancer Res., Royal Cancer Hosp., Fulham Rd., London SW3, England); Hewer, A.; Walsh, C.; Grover, P. L.; Sims, P. *Chem Biol Interact* 18(2): 179-193; 1977.

Experiments with Chester Beatty and C57 Bl male mice indicated that the reactive intermediate in the metabolic activation of 7-methylbenz(a)anthracene is 3,4-dihydro-3,4-dihydroxy-7-methylbenz(a)anthracene 1,2-oxide. This finding supports the hypothesis that vicinal diol-epoxides are the active intermediates of polycyclic hydrocarbons. (30 refs.)

77-4361 **Metabolic Activation of Polycyclic Hydrocarbons. Fluorescence Spectral Evidence Is Consistent with Metabolism at the 1,2- and 3,4-Double Bonds of 7-Methylbenz[a]anthracene.** (Eng.) Vigny, P. (Fondation Curie-Institut du Radium, Laboratoire Curie, 11, Rue Pierre et Marie Curie, 75231, Paris, Cedex 05, France) Duquesne, M.; Coulomb, H.; Lacombe, C.; Tierney, B.; Grover, P. L.; Sims, P. *FEBS Lett* 75(1): 9-12; 1977.

The metabolic activation of 7-methylbenz(a)anthracene (MBA) was studied by recording the DNA fluorescence emission spectra using a photon-counting spectrophotofluorimeter. Spectra were obtained from DNA treated with 3,4-dihydro-3-dihydroxy-7-methylbenz(a)anthracene 1,2-oxide (I) or 8,9-dihydro- 8,9- dihydroxy -7-methylbenz(a)anthracene 10,11-oxide (II) or DNA isolated from hamster embryo cells or mouse skin following treatment with MBA (1 μM or 1 μg/ml acetone, respectively). The results show that the hydrocarbon moieties that become bound to DNA in hamster embryo cells and in mouse skin treated with MBA have spectral characteristics that are similar to those of DNA that has been reacted in solution with I. However, they are quite different from those of DNA that has been treated with II. These results are consistent with the hypothesis that vicinal diol epoxides are important in the metabolic activation of polycyclic hydrocarbons. They indicate that with MBA, the active metabolite is compound I. (16 refs.)

77-4362 **The Effect of Dimethylbenz(a)anthracene on Murine Hematopoiesis.** (Eng.) Seidel, H. J. (Dept. Clinical Physiology, Center Basic Clinical Res., Univ. Ulm, Oberer Eselsberg, D-7900 Ulm/Donau, Germany) *Z Krebsforsch* 89(2): 221-229; 1977.

The effects of dimethylbenz(a)anthracene (DMBA) on hematopoietic stem cells were investigated in young adult female CBA/J mice given a single 1-mg dose po or four 1-mg doses po in weekly intervals. In the peripheral blood, both regimens induced only a transient reticulocytopenia and thrombocytopenia. With four doses the thymus and spleen wts were reduced up to 4 wk after the last dose. Bone marrow cellularity was lower in treated animals than in controls. After 1 mg DMBA, pluripotent stem cells (colony-forming units, CFUs) in the marrow were reduced to 50%-70% of control values over a 2- to 3-wk period; in the spleen the CFU concentration was reduced to 10% at day 3, with a return to normal levels after 3-4 wk. The region of granulocytic committed stem cells (CFUc) in both organs followed the same pattern with an overshoot in CFUc concentration in the spleen after 3-4 wk. After four doses, CFUs and CFUc were more depressed, but regeneration began about 2 wks after the last dose in both organs. Within 3-4 wk of the last dose, CFUc concentrations were normal in the marrow and supranormal in the spleen. The effect of DMBA on stem cells was similar to that of ionizing radiation and of methylnitrosourea. (11 refs.)

77-4363 **Cultivation of Human Adult Fibroblasts and an Attempt to Induce Malignant Transformation with 7,12-Dimethylbenz(a)anthracene (Meeting Abstract).** (Eng.) Kesava Rao, K. V. (Biology Div., Cancer Res. Inst., Tata Memorial Centre, Parel, Bombay 400 012 India) Bhat, A. V.; Bapat, C. V. *In Vitro* 13(3): 184; 1977. (no refs.)

77-4364 Early Esterase Changes in Skin of Mice Exposed to the Carcinogen, **7,12-Dimethylbenz(a)anthracene (Meeting Abstract).** (Eng.) Tyndall, R. (Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830) Jones, J.; Bracken, W. *Proc Am Assoc Cancer Res* 18: 73; 1977. (no refs.)

77-4365 **Hamster Cells, Untreated and Treated with Chemical Carcinogens, Maintained In Vitro for 2 1/2 Years.** (Eng.) Papadopoulo, D. (Foundation Curie-Institut du Radium, Section de Biologie, 26 rue d'Ulm, 75005 Paris, France) Levy, S.; Chamaillard, L.; Beesau, O.; Hubert-Habart, M.; Markovits, P. *Br J Cancer* 36(1): 65-71; 1977.

The properties of untreated hamster whole embryo, fetal brain, and neonate lung cells maintained in culture for 1-2.5 yr were compared with those of cells transformed by the following chemical carcinogens: 7,10-dimethylbenzo(c)acridine, benzo(a)pyrene, 7,12-dimethylbenzo(a)anthracene, 7-methylbenz(a)anthracene, 3-methylcholanthrene, and 2-chlorobutadiene. Among the seven untreated lines studied, only one spontaneous transformation was observed during the first year of culture. The cells of the six other lines remained normal and diploid and were not transplantable during the first 9 to 12 mo of culture. After 12 mo, changes appeared in their in vitro behavior and their transplantability: grafts of 0.5-2 × 10^6 cells induced tumors in the hamster; fewer cells did not. In vitro chemically transformed hamster cells were fundamentally different from untreated cells of the same origin, not only in morphological and growth characteristics but also in transplantability. Of the nine lines obtained, seven induced tumors after injection of 10^1-10^4 cells and two after injection of 10^5 cells per animal. (15 refs.)

77-4366 **The Nature of Benzo(a)pyrene-DNA Adducts Formed in Hamster Embryo Cells Depends on the Length of Time of Exposure to Benzo(a)pyrene.** (Eng.)

aird, W. M. (Wistar Inst. Anatomy and Biology, 36th St. Spruce, Philadelphia, PA 19104) Diamond, L. *Biochem iophys Res Commun* 77(1): 162-167; 1977.

dducts of benzo(a)pyrene (BP) with DNA were analyzed ter the exposure of Syrian hamster embryo cells to tritiated P for varying lengths of time. Analysis was directed at disnguishing between adducts derived from the syn-isomer of P-7,8-diol-9,10-epoxide [(±)7α,8β-dihydroxy-9α,10α- ooxy-7,8,9,10-tetrahydro-BP] and the anti-isomer [(±)7α,8 -dihydroxy-9β,10β-epoxy-7,8,9 10-tetrahydro-BP]. After 4 nd 6 hr, anti-isomer derivatives were present in slight excess; ter 72 hr, anti-isomer adducts were 1.4-fold more abundant ıan syn-isomer adducts. Both diol-epoxide isomers play an nportant role in the binding of BP to DNA in this system, nd the nature of the relative amount of BP-DNA adducts ound depends upon the length of exposure to BP. (23 refs.)

7-4367 **The Interactions of Benzo(a)pyrene with Mouse Epithelial Cells in Culture (Meeting Abstract).** Eng.) Landolph, J. R. (Univ. California, Berkeley, CA 4720). *Diss Abstr Int [B]* 38(2): 651-652; 1977. (no refs.)

7-4368 **Enzymatic Formation and Properties of a Conjugate of Sulfate with 3-Iydroxybenzo(a)pyrene.** (Eng.) Nemoto, N. (Dept. Experiıental Pathology, Cancer Inst., 1-37-1, Kami-Ikebukuro, 'oshima-ku, Tokyo, Japan) Takayama, S. *Biochem Pharıacol* 26(7): 679-684; 1977.

t was demonstrated that the 105,000-g supernatant fraction om rat liver is able to catalyze the formation of the sulfate onjugate of 3-hydroxybenzo(a)pyrene (30H-BP). On excitaon at 385 nanometers (nm), peaks of fluorescence of the onjugate of 3-hydroxybenzo(a)pyrene (3-OH-BP). On xcitation at 385 nanometers (nm), peaks of fluoresence of the conjugate were seen at 415 and 435 nm in queous ethanol. The amount of conjugate formed deended on the amount of supernatant used and the eriod of incubation; ATP could not be replaced by MP, GTP, or GMP. The sulfate conjugate was less polar ıan the glutathione and glucuronide conjugates of -OH-BP. It was more stable than the sulfate conjugate f N-acetylaminofluorene, which is thought to be an ltimate carcinogen. The sulfate conjugate of 3-OH-BP ıay play a role in the detoxification of 3-OH-BP or in ıe transport of 3-OH-BP from the liver to target organs. 23 refs.)

7-4369 **Carcinogenic Activity of Anthanthrene on Mouse Skin.** (Eng.) Cavalieri, E. (Eppley Inst. es. Cancer, Univ. Nebraska Medical Center, Omaha, NB 8105) Mailander, P.; Pelfrene, A. *Z Krebsforsch* 89(2): 113-18; 1977.

ibenzo(cd,jk)pyrene (anthanthrene), considered to be noncarcinogenic, was examined for carcinogenicity in a comparative study with other polycylic hydrocarbons. Anthanthrene induced benign and malignant epidermal neoplasms in female Swiss mice after repeated skin application (0.396 micromole twice weekly for 30 wk). The incidence of these tumors (47%) was lower and the latency longer than that of those found after treatment with corresponding molar amounts of benzo(a)pyrene or dibenzo(a,h)pyrene. Since the proportion of malignant neoplasms was similar (60%) in these three groups, the results indicate that anthanthrene is a relatively strong carcinogen. A rationale accounting for previous negative results in percutaneous experiments with this compound is suggested. (11 refs.)

77-4370 **Accelerating Action of Tea on Mouse Skin Carcinogenesis.** (Eng.) Bogovski, P. (Inst. Experimental and Clinical Medicine, 42 Hiiu St., Tallinn, Estonia 200015, USSR) Day, N. *Cancer Lett* 3(1/2): 9-13; 1977.

The effect of different tannin-containing aqueous solutions on the carcinogenic action of 0.53-0.6 mg benzo(a)pyrene (BP) on the skin of Charles River CD-1 mice was investigated. Tumor appearance was accelerated in mice treated with either tea or an oak extract containing 1% tannin after a single application of BP. The time of tumor appearance in mice treated with gallic acid or tannic acid after treatment with BP was similar to that in the group treated with BP alone. The overall incidence of tumor (30%-36%) was similar in all five groups. (8 refs.)

77-4371 **Determination of Benzo(a)pyrene in Protein-Vitamin Concentrates and in the Raw Material from Which They Are Produced.** (Eng.) Goriaev, M. N. (Inst. Chemical Sciences, Acad. Sciences Kazakh SSr, Alma-Ata, USSR) Artamonov, A. F.; Popova, E. B.; Miasnikov, A. I. *Izv Akad Nauk Kazakh SSR Ser Khim* (6): 65-66; 1976.

The content of benzo(a)pyrene (BP) in nutrient yeast (protein-vitamin complexes) was found to be 10^{-8} g/g by luminescence spectrometry. It is suggested that raw materials slated for eventual consumption should undergo purification to remove any polycyclic aromatic hydrocarbons. (4 refs.)

77-4372 **Pulmonary Tumorigenesis in Syrian Golden Hamsters after Intratracheal Instillations with Automobile Exhaust Condensate.** (Eng.) Reznik-Schuller, H. (Abteilung fur Experimentelle Pathologie, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, 3000 Hannover 61, W. Germany) Mohr, U. *Cancer* 40(1): 203-210; 1977.

Automobile exhaust condensate, at doses of 2.5 or 5 mg, was instilled intratracheally once every 2 wk for life in Syrian golden hamsters. The condensate was prepared from the most common German passenger car driven in the Europa-Test cycle (simulated city driving), and it contained 340 μg/g benzo(a)pyrene (BP). Despite the very low total dose of BP received, all animals of both dosage groups developed multiple pulmonary adenomas. Electron microscopy revealed that these tumors resembled BP-induced pulmonary adenomas. Numerous condensate-laden macrophages in tumor and peripheral lung tissues indicated that little of the instilled condensate had been removed from the airways through mucociliary action. (29 refs.)

77-4373 **The Effects of Cigarette Smoke on the Metabolism of Benzo(a)pyrene in Perfused Rat Lung (Meeting Abstract).** (Eng.) Vahakangus, K. (Dept. Pharmacology, Univ. Oulu, SF-90220 Oulu 22, Finland); Nevasaari, K.; Pelkonen, O.; Karki, N. T. *Acta Pharmacol Toxicol [Suppl] (Kbh)* 41(4): 78; 1977. (no refs.)

77-4374 **The Ability of Enteric Bacteria to Catalyze the Covalent Binding of Bile Acids and Cholesterol to DNA and Their Inability to Metabolize Benzo(a)pyrene to a Binding Product and to Known Metabolites.** (Eng.) Zachariah, P. K. (Faculty Pharmacology, Memorial Univ. Newfoundland, Saint Johns, Newfoundland, Canada) Slaga, T. J.; Berry, D. L.; Bracken, W. M.; Buty, S. G.; Martinsen, C. M.; Juchau, M. R. *Cancer Lett* 3(1/2): 99-105; 1977.

The capacity of enteric bacteria (*Escherichia coli*, Salmonella, Pseudomonas, Shigella, and Klebsiella) to catalyze the covalent binding of benzo(a)pyrene (BP), cholic acid, deoxycholic acid and cholesterol was investigated. In general, these bacteria were incapable of activating BP to a covalently bound product with calf thymus DNA. Metabolism studies of BP by fluorometric assay failed to indicate any accumulation of BP-3-hydroxy in the incubation medium. Detailed metabolic investigation with high-pressure liquid chromatography indicated that bacteria did not produce any known metabolites formed by mammalian systems. However, radioactivity was detected in all fractions, suggesting that the bacteria were readily metabolizing BP into smaller molecules for energy and carbon sources. Although the enteric bacteria did not metabolize BP, some activated cholesterol, cholic acid, and deoxycholic acid to covalently bound products with DNA. The binding data with cholesterol and bile acids suggested that the binding process required NADPH as a cofactor, because the binding level was rather low without NADPH. (26 refs.)

77-4375 **Differences in Benzo(a)pyrene Metabolism Between Lung and Liver Homogenates.** (Eng.) Kimura, T. (Biophysics Div., Natl. Cancer Center Res. Inst., Tokyo 104, Japan) Kodama, M.; Nagata, C. *Biochem Pharmacol* 26(7): 671-674; 1977.

The metabolism of ^{3}H-benzo(a)pyrene (BP) was studied in both liver and lung homogenates from untreated Sprague-Dawley rats and from rats pretreated with 3-methylcholanthrene (MC) or phenobarbital (PB). Electron spin resonance studies demonstrated that BP metabolism by the lung homogenates from untreated and PB-treated rats yields a max peak at 440 nanometers that is not seen on metabolism by liver homogenates from PB- or MC-treated rats. This peak may result from 9-hydroxy-BP. Although the 6-oxy-BP radical was formed on metabolism by liver homogenates from untreated and PB- and MC-treated rats, a different species of free radical was formed on metabolism by lung homogenates from untreated and PB- and MC-treated rats. (7 refs.)

77-4376 **Metabolism of Benzo(a)pyrene (BP) by Human Peripheral Blood Monocytes and Lymphocytes (Meeting Abstract).** (Eng.) Vaught, J. B. (Roswell Park Memorial Inst., Buffalo, NY 14263); Gurtoo, H. L.; Paigen, B.; Minowada, J.; Sartori, P. *Pharmacologist* 19(2): 191; 1977. (no refs.)

77-4377 **The Effect of Dietary Lipids on 3,4-Benzo(a)pyrene Metabolism in the Hepatic Endoplasmic Reticulum.** (Eng.) Lambert, L. (Dept. Biochemistry, Medical Coll. St. Bartholomew's Hosp., Charterhouse Square, London E.C.1M 6BQ, England) Wills, E.D. *Biochem Pharmacol* 26(15): 1423-1427; 1977.

The effects of changing the nature of dietary lipids on the hydroxylation of benzo(a)pyrene (BP) by rat liver microsomes were studied. A comparison was made of the effects of similar dietary factors on the oxidative metabolism of drugs such as aminopyrene. BP-hydroxylation was minimal when a fat-free diet was fed, little affected by the addition of 10% lard (containing mainly saturated and monounsaturated fatty acids, but only 6% linoleic acid), but increased to a significant extent by 10% corn oil (containing 50% linoleic acid). The addition of 10% herring oil (containing 15.4% polyunsaturated fatty acids but only 1.7% linoleic acid) to the diet did not increase the hydroxylation rate. Methyl linoleate increased the hydroxylation rate significantly, vitamin E did not affect it, and cholesterol was inhibitory in some tests. The oxidative demethylation of the drugs was also enhanced by a supply of dietary linoleic acid. However, cholesterol and vitamin E, which stimulate oxidative demethylation, do not significantly affect BP hydroxylation, demonstrating that membranes of different structures may be required for max activity of the two enzyme systems. (17 refs.)

77-4378 **Utilization of *Salmonella typhimurium* Mutants to Assess the Possibility of the Photody-**

namic Action of 3,4-Benzopyrene on DNA (Meeting Abstract). (Ita.) Marchi, C. (Istituto di Microbiologia, Universita di Siena, Siena, Italy); Coratza, G.; Molina, A. M. *Ann Sclavo* 18(6): 892-893; 1976. (no refs.)

77-4379 **Influence of Pretreatment on B(a)P Metabolism in the Isolated Perfused Lung (Meeting Abstract).** (Eng.) Niemeier, R. (Univ. Cincinnati Coll. Medicine, Dept. Environmental Health, Cincinnati, OH); Warshawsky, D.; Bingham, E. *Toxicol Appl Pharmacol* 41(1): 185; 1977. (no refs.)

77-4380 **Mutagenicity of the Optical Enantiomers of the Diastereomeric Benzo[a]pyrene (BP) 7,8-Diol-9,10-Epoxide (Meeting Abstract).** (Eng.) Chang, R. L. (Hoffmann-La Roche, Inc., Nutley, NJ 07110); Wood, A. W.; Levin, W.; Yagi, H.; Jerina, D. M.; Conney, A. H. *Pharmacologist* 19(2): 191; 1977. (no refs.)

77-4381 **The Mechanism of Hydrolysis of the Non-K-Region Benzo[a]pyrene Diol Epoxide r-7,t-8-dihydroxy-t-9,10 -oxy- 7,8,9,10-tetrahydrobenzo[a]-pyrene.** (Eng.) Yang, S. K. (Chemistry Branch, NCI, NIH, Bethesda, MD 20014) McCourt, D. W.; Gelboin, H. V. *J Am Chem Soc* 99(15): 5130-5134; 1977.

The kinetics of hydrolysis of benzo[a]pyrene diol epoxide r-7, t-8-dihydroxy-t-9,10-oxy-7, 8, 9, 10-tetrahydrobenzo-[a]pyrene, a potent mutagen and possibly the ultimate carcinogenic form of benzo[a]pyrene, was analyzed. A prior equilibrium of the hydrogen bonding of the diol epoxide with an acid was followed by a proton transfer to form a benzylic carbonium ion at C(10). (19 refs.)

77-4382 **Malignant Transformation and Mutagenesis in Mammalian Cells Induced by Vicinal Diol-Epoxides Derived from Benzo(a)pyrene.** (Eng.) Marquardt, H. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021) Baker, S.; Grover, P. L.; Sims, P. *Cancer Lett* 3(1/2): 31-36; 1977.

Benzo(a)pyrene (BP) and the syn- and anti-isomers of the 7,8-diol 9,10-oxide and of the 9,10-diol 7,8-oxide derived from this hydrocarbon were tested for their abilities to induce malignant transformation in M2 mouse fibroblasts and mutagenesis in V79 Chinese hamster cells. The anti-isomer of the 7,8-diol 9,10-oxide induced more mutations and transformation than did the other three vicinal diol epoxides. The two 9,10-diol 7,8-oxides were moderately mutagenic but did not induce any transformation. In contrast, BP induced transformation in M2 fibroblasts but was not mutagenic in the V79 cells. (21 refs.)

77-4383 **Enzymatic Mechanism of Benzo(a)pyrene Conversion to Phenols and Diols and an Improved High-Pressure Liquid Chromatographic Separation of Benzo(a)pyrene Derivatives.** (Eng.) Yang, S. K. (Chemistry Branch, NCI, NIH, Bethesda, MD 20014) Roller, P. P.; Gelboin, H. V. *Biochemistry* 16(16): 3680-3687; 1977.

Each of the three trans-diols formed metabolically from benzo(a)pyrene (BP) are optically pure (-) enantiomers. Studies of the oxygenation mechanism indicate that both the microsomal mixed-function oxidases and epoxide hydratase are stereospecific in the metabolism of BP to trans-diols. (52 refs.)

77-4384 **A DNA Strand Scission by Benzo(a)pyrene Diol Epoxides.** (Eng.) Gamper, H. B. (Lab. Chemical Biodynamics, Lawrence Berkeley Lab., Univ. California, Berkeley, CA 94720) Tung, A. S.; Straub, K.; Bartholomew, J. C.; Calvin, M. *Science* 197(4304): 671-674; 1977.

The reaction of the *syn*- and *anti*-benzo(a)pyrene (BP) diol epoxides (DE) with covalently closed, superhelical, *Escherichia coli* plasmid Col E1 DNA was characterized. When the DNA was reacted with either DE in tris-CHl buffer, gel electrophoresis showed substantial nicking of the DNA. A minimum DE:DNA ratio of 0.01 was required. At higher ratios, nicking increased until no DNA remained. When the DNA was reacted with the *anti* isomer, electron microscopy showed that relaxed circles result from a ratio of 0.5, linear segments of random length from a ratio of 5. At higher ratios, fragmentation was increased, suggesting that nicks are occurring at many sites around the molecule. This strand scission represents < 1% of the DNA modification by DE. By scaling up the reaction mixtures fiftyfold and using ^{14}C-labeled anti-DE, the relative frequency of strand scission was estimated. At a DE:DNA ratio of 0.5, there were 310 adducts per DNA molecule; at a ratio of 0.05, there were 47 adducts per molecule. In studies of the kinetics of DNA nicking by DE, the rapidity with which nicking followed adduct formation was not typical of depurination or depyrimidination strand scission. Each DNA molecule was nicked an av of one time, and the entire relaxation process was complete in 4 hr. The most likely reason for this rapid nicking is the facile hydrolysis of phosphotriesters formed by the DE. If confirmed, the formation of unstable deoxyribophosphotriesters by BP is unique. The low frequency of phosphotriester formation in vitro does not preclude their existence in vivo, where they may be involved in the highly mutagenic and potentially carcinogenic activity of DE. (30 refs.)

77-4385 **A Comparison of Benzopyrene Metabolism by 3-Methylcholanthrene-induced and Non-induced Liver and Lung Enzymes from the Rhesus Monkey, Evaluated by High-pressure Liquid Chromatography (Meeting Abstract).** (Eng.) Freudenthal, R. I. (Battelle's Columbus

Lab., Columbus, OH); Hundley, S. G. *Toxicol Appl Pharmacol* 41(1): 214-215; 1977. (2 refs.)

77-4386 **Effect of Phenobarbital and 3-Methylcholanthrene Administration on Epoxide Hydrase Levels in Liver Microsomes.** (Eng.) Bresnick, E. (Dept. Cell and Molecular Biology, Medical Coll. Georgia, Augusta, GA 30902) Mukhtar, H.; Stoming, T. A.; Dansette, P. M.; Jerina, D. M. *Biochem Pharmacol* 26(9): 891-892; 1977.

The effects of prior administration of phenobarbital (PB) or 3-methylcholanthrene (3-MC) on the ability of Sprague-Dawley liver microsomes to catalyze the hydration of a series of oxides are presented. The rats were injected ip with PB (75 mg/kg) in saline, 3-MC (20 or 40 mg/kg) in corn oil, or with the vehicles alone every 24 hr. The rats were sacrificed 24 hr after the last injection, and epoxide hydrase activity was determined. PB increased the specific activity of the hydrase(s) toward styrene oxide (134%), naphthalene oxide (171%), octene oxide (152%), and 3-MC 11,12-oxide (133%). At 20 mg/kg, 3-MC increased the hydration of octene oxide by 29% after 48 hr; at 40 mg/kg, this hydration was elevated by 40% after 72 hr. The hydrations of styrene oxide, naphthalene oxide, and 3-MC 11,12-oxide were unaffected by 20 mg/kg 3-MC at 48 hr. However, in other experiments with 40 mg/kg 3-MC, approx 50% increases in epoxide hydrase activity toward octene oxide or 3-MC 11,12-oxide were noted at 72 hr. The data show that prior exposure of animals to certain drugs may result in an increase in their ability to form potentially pharmacologically active *trans*-dihydrodiol derivatives of polycyclic hydrocarbons. Therefore, regulation of epoxide hydrase activity may be an important determinant in the carcinogenic process. (29 refs.)

77-4387 **Transplacental Induction of Mixed-Function Oxygenases in Extra-hepatic Tissues by 2,3,7,8-Tetrachlorodibenzo-p-dioxin.** (Eng.) Berry, D. L. (Dept. Pharmacology, Sch. Medicine, Univ. Washington, Seattle, WA 98195) Slaga, T. J.; Wilson, N. M.; Zachariah, P. K.; Namkung, M. J.; Bracken, W. M.; Juchau, M. R. *Biochem Pharmacol* 26(15): 1383-1388; 1977.

A study was made of the induction of aryl hydrocarbon hydroxylase (AHH) activity in the hepatic and extrahepatic tissues of both fetuses and mother rats following exposure of pregnant Sprague-Dawley rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Further study was made of the ability of the various tissues to metabolize benzo(a)pyrene (BP). On day 20, following a single ip dose of 6.0 μg/kg TCDD on day 17 of gestation, AHH was induced 24-, 22-, 60-, and 4-fold in fetal lung, kidney, liver, and skin, respectively; maternal lung, kidney, liver and adrenal AHH was increased 4-, 2-, 30-, and 2-fold, respectively. High-pressure liquid chromatographic analysis of BP metabolism after TCDD induction indicated that fetal lung, kidney, and skin produced significant quantities of BP-7,8-diol, BP-4,5-diol, and the 9- and 3-phenols of BP. Maternal lung also produced BP-9,10-diol but maternal adrenal gland yielded primarily the 9-phenol of BP. Epoxide hydratase activity was increased two- to threefold in maternal lung, fetal lung, and skin after TCDD pretreatment, but was not affected significantly in liver, kidney, or placenta. It is concluded that TCDD provides a potent and broad-spectrum transplacental induction of carcinogen-transforming enzymes in extrahepatic tissues. (41 refs.)

77-4388 **The Effects of Antioxidants on Skin Tumor Initiation and Aryl Hydrocarbon Hydroxylase.** (Eng.) Slaga, T. J. (Biology Div., Oak Ridge Natl. Lab., Post Office Box Y, Oak Ridge, TN 37830) Bracken, W. M. *Cancer Res* 37(6): 1631-1635; 1977.

The inhibitory effect of antioxidants on CD1 mouse skin tumorigenesis initiated with 7,12-dimethylbenzanthracene (DMBA: 2.56 μg) and promoted 1 wk later with 12-O-tetradecanoyl (AHH) in this inhibition were studied. The following antioxidants did not induce epidermal AHH significantly or have any effect on AHH activity in vitro: butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), vitamin C, and vitamin A, all at concentration of 1 or 2×10^{-4} M. However, BHA and BHT were able to inhibit the in vitro covalent binding of benzo(a)pyrene (BP) and DMBA to the DNA of epidermal cell homogenates when applied topically 3 or 12 hr prior to death. They did not inhibit binding when added to the homogenate in vitro. The inhibition consequent on in vivo application could stem from prevention of the activation of BP and DMBA to epoxides and/or other reactive metabolites or from an increased detoxification of reactive metabolites. (33 refs.)

77-4389 **Conversion of Procarcinogens to Mutagens by Enzymes in Human Fetal and Placental Tissues (Meeting Abstract).** (Eng.) Jones, A. H. (Dept. Pharmacology, Univ. Washington Sch. Medicine, Seattle, WA 98195); Juchau, M. R. *Pharmacologist* 19(2): 201; 1977. (no refs.)

77-4390 **Ontogenetic Expression of Polycyclic Aromatic Compound-inducible Monooxygenase Activities and Forms of Cytochrome P-450 in Rabbit. Evidence for Temporal Control and Organ Specificity of Two Genetic Regulatory Systems.** (Eng.) Atlas, S. A. (Developmental Pharmacology Branch, Natl. Inst. Child Health and Human Development, NIH, Bethesda, MD 20014) Boobis, A. R.; Felton, J. S.; Thorgeirsson, S. S.; Nebert, D. W. *J Biol Chem* 252(13): 4712-4721; 1977.

Several parameters were studied in the liver microsomes of control and 3-methylcholanthrene (MC)-treated New Zealand White rabbits at various stages of development from 5 days before birth to adulthood (110 days of age). They included the complement of microsomal proteins as visualized by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, cytochrome P-450 content, and five monooxygenase activities. MC induced 2-acetylaminofluorene N-hydroxylase in rabbits aged ≥ 10 days; the induction correlated with the increase in a microsomal protein of molecular wt 54,000 daltons. MC induced aryl hydrocarbon hydroxylase (AHH) and biphenyl-2-hydroxylase only in fetuses and in neonates <12 days old; the induction correlated with the increase in a 57,000-dalton microsomal protein. Similarly, 7-ethoxycoumarin O-deethylase was induced by MC only in fetuses and neonates; it was decreased 40%-60% in older rabbits. This decreased activity paralleled the decrease in an electrophoretic band of molecular wt 50,000 daltons. Although induction of AHH by MC only occurred in the livers of rabbit fetuses or neonates, AHH remained inducible in the kidneys, lungs, and spleens of rabbits throughout adulthood. The induction correlated, as in liver, with the increase of a 57,000-dalton species. However, in the extrahepatic tissues the increase in this species was always associated with a blue spectral shift of 2 nanometers in the Soret peak of the reduced hemoprotein/carbon monoxide peak. This shift was not associated with the 57,000-dalton species induced in liver. (52 refs.)

77-4391 **The Occurrence of Cytochrome P-450 and Aryl Hydrocarbon Hydroxylase Activity in *Drosophila melanogaster* Microsomes, and the Importance of This Metabolizing Capacity for the Screening of Carcinogenic and Mutagenic Properties of Foreign Compounds.** (Eng.) Baars, A. J. (Dept. Pharmacology, Subfaculty Pharmacy, Univ. Leiden, Leiden, Netherlands) Zijlstra, J. A.; Vogel, E.; Breimer, D. D. *Mutat Res* 44(2): 257-268; 1977.

The cytochrome P-450-mediated mixed function oxidase system (including aryl hydrocarbon hydroxylase) was investigated with the use of benzo(a)pyrenes as a substrate. The activity was NADPH-dependent; it was absent when NADH was a cofactor and when microsomes were destroyed by boiling or treatment with deoxycholate. (37 refs.)

77-4392 **NADH-dependent Aryl Hydrocarbon Hydroxylase in Rat Liver Mitochondrial Outer Membrane (Meeting Abstract).** (Eng.) Uemura, T. (Istituto de Farmacologia, Universita di Milano, Milan, Italy); Chiesara, E. *Ital J Biochem* 26(1): 72-73; 1977. (no refs.)

77-4393 **Effects of Single and Repeated Cigarette Smoke-Exposures on the Activities of Aryl Hydrocarbon Hydroxylase, Epoxide Hydratase and UDP Glucuronosyltransferase in Rat Lung, Kidney and Small Intestinal Mucosa.** (Eng.) Uotila, P. (Dept. Physiology, Univ. Turku, SF-20520 Turku 52, Finland) *Res Commun Chem Pathol Pharmacol* 17(1): 101-114; 1977.

Single exposure to cigarette smoke for 1 hr decreased the pulmonary microsomal epoxide hydratase activity in male Wistar rats. A more rapid decrease was seen after five consecutive exposures of 1 hr/day. The pulmonary aryl hydrocarbon hydroxylase (AHH) activity, however, increased severalfold. In the small intestinal mucosa, the activities of AHH and epoxide hydratase were enhanced by both single and repeated cigarette smoke exposures. In the kidney, the AHH activity increased, but that of epoxide hydratase and uridine diphosphate glucuronosyltransferase was unchanged. After repeated smoke exposures, the activity of UDP glucuronosyltransferase increased in the small intestinal mucosa, but no clear change was detected in the lung. The results indicate that the smoke components responsible for AHH induction can be absorbed into the circulation and transported to the kidney, but those components responsible for epoxide hydratase induction in the intestine probably cannot reach the kidney. (33 refs.)

77-4394 **Smoke Exposure of Rodents: Correlation Between Renal Aryl Hydrocarbon Hydroxylase Activity and Mutagenesis in *S. Typhimurium* (Meeting Abstract).** (Eng.) Bilimoria, M. A. (Pathology Inst., McGill Univ., Montreal, Quebec, Canada); Johnson, J.; Hogg, J. C.; Witschi, H. P. *Toxicol Appl Pharmacol* 41(1): 198; 1977. (no refs.)

77-4395 **Activation of 2-Aminoanthracene to Mutagenic Intermediates by Guinea Pig Kidney Microsomal Enzymes Following Tobacco Smoke Inhalation.** (Eng.) Bilimoria, M. H. (Pathology Inst., McGill Univ., Montreal, Canada) Johnson, J.; Hogg, J. C.; Witschi, H. P. *Toxicol Appl Pharmacol* 41(1): 119-122; 1977.

Studies with rats and guinea pigs indicated that aryl hydrocarbon hydroxylase may be induced in the kidneys of these animals by tobacco smoke. The 9,000 x g supernatant from the kidneys of smoke-exposed guinea pigs had a greater potential for activating 2-aminoanthracene into mutagenic intermediates than that from normal kidneys. (11 refs.)

77-4396 **Partitioning of Polycyclic Aromatic Hydrocarbons Between Dissolved and Particulate Phases in Natural Waters.** (Eng.) Herbes, S. E. (Environmental Sciences Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830) *Water Res* 11(6): 493-496; 1977.

A study was made to quantitate the adsorption characteristics of a representative polycyclic aromatic hydrocarbon (PAH) onto organic particulate matter and to identify critical adsorption parameters. The results showed that a significant fraction of anthracene and other PAH compounds in dissolved and particulate forms would be found in natural waters. (17 refs.)

77-4397 **Sub-Part-per-Trillion Detection of Polycyclic Aromatic Hydrocarbons by Laser Induced Molecular Fluorescence.** (Eng.) Richardson, J. H. (General Chemistry Div., Lawrence Livermore Lab., Univ. California, Livermore, CA 94550) Ando, M. E. *Anal Chem* 49(7): 955-959; 1977.

The intensity of characteristic fluorescence emissions from representative polycyclic aromatic hydrocarbons at various concentrations in aqueous solutions was measured by laser-induced molecular fluorescence (LIMF). The detection limits for benzene, naphthalene, anthracene, fluoranthene, and pyrene were found to be 19 ppb and 1.3, 4.4, 1.0, and 0.5 parts per trillion, respectively. The fluorescence of each of these substances demonstrated a linear dependence on concentration, sometimes extending over a concentration range of six orders of magnitude. LIMF is a sensitive and selective technique for measuring of polycyclic hydrocarbon levels. Its use should prove of value to those areas of biochemistry, pollution monitoring, and chemical reaction mechanistic and kinetic studies that require sensitive analytical methods. (30 refs.)

77-4398 **Analogues of Anthracene, Phenanthrene, and Benzoflavone Inhibit Prostaglandin Biosynthesis by Cells in Culture.** (Eng.) Levine, L. (Dept. Biochemistry, Brandeis Univ., Waltham, MA 02154) Hong, S. L. *Prostaglandins* 14(1): 1-9; 1977.

Prostaglandin production by methylcholanthrene-transformed 3T3 mouse fibroblasts (MC5-5), human normal fibroblasts (D550), and canine kidney (MDCK) cells was inhibited by several analogs of anthracene, phenanthrene, and benzoflavone. Among the most effective inhibitors of MC5-5 prostaglandin production were anthracene [median infective dose (ID50), 1.7 μM], 9,10-diaminophenanthrene (ID50, 0.48 μM), and 7,8-benzoflavone (ID50 0.55 μM). Under identical conditions, the ID50's for indomethacin and aspirin were 0.049 and 8.9 μM, respectively. Production of radioactive prostaglandins by MC5-5 cells from tritiated phospholipids was blocked by 18 μM 7,8-benzoflavone, but this compound did not block the release of radioactive arachidonic acid. In fact, 7,8-benzoflavone increased the release of radioactive arachidonic acid from the cells. (8 refs.)

77-4399 Mass Spectrometry of Cyclopenta[a]-phenanthrenes. Metabolites Formed in Vitro **and In Vivo from the Carcinogen 15,16-Dihydro-11-methylcyclopenta[a]phenanthren-17-one.** (Eng.) Vose, C. (Dept. Metabolic Studies, G. D. Searle & Co. Ltd., Lane End Road, High Wycombe, HP12 4HL, Buckinghamshire, England) Coombs, M. M. *Biomed Mass Spectrom* 4(1): 48-51; 1977.

The mass spectra of several synthetic cyclopenta(a):phenanthrenes, including the parent ketone, which is inactive, and 15,16-dihydro-11-methylcyclopenta(a)phenanthren-17-one (1a), a potent carcinogen, are reported. A metabolite of 1a was isolated in an in vitro metabolism experiment and purified. Accurate mass measurement of the molecular ion gave the molecular formula $C_{18}H_{14}O_2$, indicating the presence of one additional oxygen atom. The high intensity of the molecular ion and generally low abundance of fragment ions proved the absence of metabolism in the D ring. This metabolite was formed by metabolism of the carcinogen in an aromatic ring or in the methyl group. In addition, the structure of the major metabolite of 1a, isolated from rat urine, was established as 8,9-epoxy-1α,2β,15ξ-trihydroxy-11-methyl-8,9- secogona-3,5,7,9,11,13-hexaen-17-one (5), with the formula $C_{18}H_{14}O_4$. The mass spectra of 5, its triacetate, and its acid dehydration product confirmed the presence of three secondary hydroxyl groups, two as part of a dihydrodiol system; a fourth oxygen atom was accounted for as a carbonyl group upon chemical and spectroscopic evidence. The fifth oxygen atom was present as a bridgehead epoxide. Mass spectral data provided initial evidence for the bridgehead epoxide in the metabolite, and they were compatible with the structure assigned to it on the basis of all chemical and spectroscopic evidence. (12 refs.)

77-4400 **Ethidium Bromide Mutagenesis in *Saccharomyces cerevisiae*: Modulation by Growth Medium Components.** (Eng.) Gardella, R. S. (Dept. Microbiology, Univ. Maryland, College Park, MD 20742) MacQuillan, A. M. *Mutat Res* 46(4): 269-284; 1977.

Several medium components, especially potassium lactate, have been found to modify the mutagenic response of *Saccharomyces cerevisiae* to ethidium bromide. Laboratory experiments using this system must adhere to strict parameters to avoid errors. (36 refs.)

77-4401 **Isolation of the Glucuronic Acid Conjugate of N-Hydroxy-4-aminobiphenyl from Dog Urine and Its Mutagenic Activity.** (Eng.) Radomski, J. L. (Dept. Pharmacology, Univ. Miami, Sch. Medicine, Miami, FL 33152) Hearn, W. L.; Radomski, T.; Moreno, H.; Scott, W. E. *Cancer Res* 37(6): 1757-1762; 1977.

Analysis of the urine of beagle dogs, in which bladder cancer was induced by the administration of 4-aminobiphenyl (4ABP: 10 mg/kg, in capsule form), revealed the presence of the glucuronic acid conjugate of N-hydroxy-4-aminobiphenyl. The conjugate was found to be an active mutagen in *Salmonella typhimurium* strains TA1538 and TA98, but not in strains TA1535 and TA1537. N-Hydroxy-4ABP and 4-nitrosobiphenyl were also highly active in TA1538 and TA98 and inactive in TA1535 and TA1537. The glucuronic acid conjugate of N-hydroxy-4ABP is suggested to be the water-soluble carrier that delivers the active carcinogenic metabolite of 4ABP to the bladder. Chemical evidence is presented that the glucuronic acid conjugates via the nitrogen atom of the hydroxylamine group of N-hydroxy-4ABP, and not via the oxygen atom. (22 refs.)

77-4402 **Carcinogenic Action of 4,4-Diaminodiphenyl Ether in Rats.** (Ger.) Steinhoff, D. (Institut fur Toxikologie der Bayer AG, D-5600 Wuppertal-Elberfeld, W. Germany) *Naturwissenschaften* 64(7): 394; 1977.

Max doses (100-300 mg/kg) of chemically pure 4,4-diaminodiphenyl ether were injected sc into 40 Wistar rats (20 males and 20 females). The total dose was 14.4 g/kg. Twenty-two rats died from malignant tumors, 10 of which were hepatic tumors. Twenty-two rats also developed benign tumors, 12 of which were in the liver. In the control group (physiological saline injected sc), 13/50 rats had malignant tumors and 10 rats had benign tumors. The control group had no hepatic tumors. (2 refs.)

77-4403 **Dephenylation of N-Phenyl-2-naphthylamine in Dogs and Its Possible Oncogenic Implications.** (Eng.) Batten, P. L. (Imperial Chemical Industries Ltd., Central Toxicology Lab., Alderley Park, Nr. Macclesfield, Cheshire SK10 4TJ, England) Hathway, D. E. *Br J Cancer* 35(3): 342-346; 1977.

When dogs received large doses of N-phenyl-2-naphthylamine (PBNA), 90% of the compound was excreted within 3 days. The extent of PBNA N-dephenylation was unaltered by chronic administration. It is suggested that the levels of 2-naphthylamine (BNA) produced by N-dephenylation of PBNA in vivo do not incur a carcinogenic risk. (15 refs.)

77-4404 **Granulomas and Cholestatic-Hepatocellular Injury Associated with Phenylbutazone. Report of Two Cases.** (Eng.) Ishak, K. G. (Dept. Hepatic Pathology, Armed Forces Inst. Pathology, Washington, DC 20306) Kirchner, J. P.; Dhar, J. K. *Am J Dig Dis* 22(7): 611-617; 1977.

Two men, aged 56 and 72 yr, each developed cholestatic-hepatocellular injury and noncaseating granulomas 1 and 4 wk, respectively, after phenylbutazone therapy. The symptoms and abnormalities regressed after cessation of the therapy. (43 refs.)

77-4405 **Short- and Long-Term Effects of a Massive Dose of 6-OH-DA upon Marsh Mice.** (Eng.) Bryson, G. (Santa Barbara Cottage Hosp. Res. Inst., Santa Barbara, CA 93105) Bischoff, F. *Res Commun Chem Pathol Pharmacol* 17(3): 411-420; 1977.

Long-term studies with male Marsh mice who received 6-hydroxydopamine (100 mg/kg sc) indicate that lymphoid tumor induction was not affected in these animals. However, these animals did develop anomalies and tumors of the liver. (8 refs.)

77-4406 **Analgesic Abuse, Renal Parenchymal Disease and Uroepithelial Carcinoma (Meeting Abstract).** (Eng.) Storey, B. G. (Dept. Urology, Sydney Hosp., Sydney, New South Wales, Australia); Ibanez, R.; Mahoney, J. F.; Stewart, J. H. *Aust NZ J Med* 7(2): 200; 1977. (no refs.)

77-4407 **Malignant Mesenchymoma and Birth Defects. Prenatal Exposure to Phenytoin.** (Eng.) Blattner, W. A. (Environmental Epidemiology Branch, A521 Landow Building, NIH, Bethesda, MD 20014) Henson, D. E.; Young, R. C.; Fraumeni, J. F. *JAMA* 238(4): 334-335; 1977.

A case is reported of malignant mesenchymoma, a soft tissue sarcoma that may arise from a defect during embryogenesis, in an 18-yr-old male born with a cleft lip and palate. Throughout her pregnancy, his mother had received 400 mg of phenytoin/day. The patient experienced a 7-yr asymptomatic period following an 18-mo period of cyclophosphamide and vincristine sulfate treatment. The patient died at the age of 26, and autopsy revealed a recurrent tumor permeating throughout the hepatic parenchyma. Because cases of neuroblastoma have also been reported in two young children with the fetal hydantoin syndrome, the possibility of transplacental carcinogenesis by phenytoin should be considered. (11 refs.)

77-4408 **Long-Term Use of Phenytoin: Effects on Bone-Marrow Chromosomes in Man.** (Eng.) Knuutila, S. (Res. Dept., Rinnekoti Institution for the Mentally Retarded, Espoo, Finland) Siimes, M.; Simell, O.; Tammisto, P.; Weber, T. *Mutat Res* 43(2): 309-312; 1977.

The bone marrow chromosomes of 22 mentally retarded epileptics (aged 4-47 yr, mean 21) who were being treated with phenytoin (PT) were examined to determine the frequency of chromosomal abnormalities. All patients had been treated with PT only for at least 6 mo, and the serum concentration varied between 4 and 113 micromoles/liter. The results were compared with those of 20 healthy controls. Of the 2,566 cells studied for chromosomal structural changes, only 2 had a chromosome-type achromatic lesion (gap) and 2 had a single acentric fragment. The frequency of chromatid-type structural aberrations ranged from 0% to 5.4% in the patients. The mean frequency of all chromosomal structural changes was 0.5% among the patients and 0.4% among the controls. No structural rearrangements were detected in 737 metaphases stained by the ASG technique. The mean frequency of hyperdiploidy and polyploidy was similar in patients and controls. A double-blind study was made of the morphology of the bone marrow cells of both groups. No megaloblastic or cytotoxic changes were observed in peripheral blood smears or in bone marrow specimens. Peripheral blood cell counts were also normal. Although the results show that PT alone in therapeutic doses is not clastogenic, the possibility exists that a combination of anticonvulsant drugs might damage chromosomes. Folate deficiency, one possible side effect of anticonvulsant drugs, could explain the cytogenetic abnormalities that some investigators have attributed to PT. (17 refs.)

77-4409 **Stimulation of Hepatic Drug Hydroxylation and Conjugation by a Cutaneously Applied PCB-Mixture (Clophen A 50).** (Eng.) Marniemi, J. (Rehabilitation Examinations Centre, Social Insurance Institution, 20720 Turku 72, Finland); Nokkala, M.; Vainio, H.; Hartiala, K. J. *Chem Biol Interact* 18(2): 247-251; 1977.

The effects of a commercial polychlorinated biphenyl, Clophen A 50, on the liver enzymes of adult male Wistar rats was investigated. The compound (4 or 8 mg/kg) was applied to the skin once daily for 3 or 6 days. Even this small amount reached the liver in concentrations sufficient to induce monooxygenation and subsequent drug metabolism. These findings stress the importance of the dermal route of exposure to harmful chemicals. (29 refs.)

77-4410 **Xenobiotic Metabolism in Skin of Hairless Mice Exposed to Ultraviolet Radiation (UV), Aroclor 1260, or Chlordane (Meeting Abstract).** (Eng.) Pohl, R. J. (Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC 27709); Fouts, J. R. *Pharmacologist* 19(2): 200; 1977. (no refs.)

77-4411 **In Vitro Mutagenicity of the Soil Nematicide 1,3-Dichloropropene.** (Eng.) Neudecker, T. (Inst. Toxicology, Versbacher Landstrasse 9, D-8700 Wurzburg, W. Germany) Stefani, A.; Henschler, D. *Experientia* 33(8): 1084-1085; 1977.

Both the cis- and trans-isomers of 1,3-dichloropropene were tested for mutagenicity using *Salmonella typhimurium.* The compound was mutagenic on strains TA 1535, TA 1537 and TA 1538. Microsomal addition decreased the amount of back mutations; the reason for this is unknown. (13 refs.)

77-4412 **A Carcinogenicity Assay of Mirex in Charles River CD Rats.** (Eng.) Ulland, B. M. (Hazleton Labs. America, Inc., 9200 Leesburg Pike, Vienna, VA 22180) Page, N. P.; Squire, R. A.; Weisburger, E. K.; Cypher, R. L. *J Natl Cancer Inst* 58(1): 133-140; 1977.

The long-term administration of 50 and 100 ppm of the organochlorine insecticide mirex in the diets of male and female Charles River CD rats was associated with a spectrum of liver lesions, from foci or areas of cellular alteration and neoplastic nodules to hepatocellular carcinoma. Statistically significant numbers of neoplastic nodules were observed in the livers of male rats receiving the high dose. Neoplastic nodules and hepatocellular carcinomas were not observed in control rats. (20 refs.)

77-4413 **Morphologic Characteristics of Hepatic Nodules Induced by Mirex and Dieldrin in Mice (Meeting Abstract).** (Eng.) Benitz, K. F. (Inst. Comparative and Human Toxicology, Albany Medical Coll., Albany, NY); Roth, R. N.; Coulston, F. *Toxicol Appl Pharmacol* 41(1): 154-155; 1977. (no refs.)

77-4414 **Mutagenicity of Dieldrin in the Salmonella-Microsome Test.** (Eng.) Majumdar, S. K. (Dept. Biology, Lafayette Coll., Easton, PA 18042) Maharam, L. G.; Viglianti, G. A. *J Hered* 68(3): 184-185; 1977.

The insecticide dieldrin was assayed for its in vitro mutagenicity in several strains of *Salmonella typhimurium.* The mutagenic activity was greatest in all strains in the presence of S-9M liver homogenate mix and less so in three strains without liver microsomes. (9 refs.)

77-4415 **Effect of Different Factors Modifying the Activity of Some Enzyme Systems of the Endoplastic Reticulum on the Sensitivity of Cell Organelles Against the Damaging Action of Chemical Agents. I: Interrelations Between the Activity of Some Enzyme Systems Located in Endoplasmic Reticulum and Hepatotoxicity of Carbon Tetrachloride.** (Eng.) Popov, S. C. (Dept. Biochemistry, Higher Inst. Zootechnics and Veterinary Medicine, Stara Zagora, Bulgaria) Yantchev, I.; Georgiev, G.; Geneva, L. *Br J Exp Pathol* 57(5): 593-603; 1976.

The interrelation between endoplasmic reticulum function and hepatotoxicity of CCl_4 was investigated, and the effects of dehydration, overheating, sleep deprivation, burning, and injections of ruthenium red or $LaCl_3$, ascites tumor, and lymphosarcoma on the sensitivity of liver cell organelles to the damaging action of chemical agents were also studied. Liver lysosomes and mitochondria of tumor-bearing rats were found to be more stable than those of control rats and showed decreased sensitivity to the damaging action of CCl_4. The mitochondria and lysosomes of burned and dehydrated rats also demonstrated resistance to the labilizing effect of CCl_4. Sleep deprivation resulted in stabilization, while overheating induced clearly expressed labilization of the biological membranes. These two factors as well as lanthanum and ruthenium red acted as antagonists of the CCl_4-produced liver cell damage. Electron microscopic examinations of hepatocytes from rats subjected to different treatments were performed. Rats treated with CCl_4 alone showed degranulation of endoplasmic reticulum, dilation of cisternae, and swollen mitochondria with low matrical density. Hepatocytes from dehydrated rats had mitochondria with high matrical density and endoplasmic reticulum with prominent lesions. Hepatocytes from dehydrated rats treated with CCl_4 had swollen mitochondria, which had lost their cristae, and endoplasmic reticulum with dilated cisternae. The hepatocytes of burned rats treated with CCl_4 had degranulated endoplasmic reticulum and a larger number of swollen mitochondria with cristae. The protective actions of these chemical, pathological, and stress factors against CCl_4-produced damage are discussed. (26 refs.)

77-4416 **Electron Microscopic Observation of the Liver in Portal Hypertension Following Chronic Exposure to Vinyl Chloride Monomer.** (Eng.) Kurokawa, S. (Nakatsugawa Municipal Hosp., Nakatsugawa-City, Gifu-Prefecture, Japan) Inagaki, T.; Okuyama, S. *Gastroenterol Jpn* 12(2): 64-69; 1977.

Two men with portal hypertension and splenomegaly following chronic exposure to vinyl chloride monomer (VCM) were studied histologically and ultrastructurally. The results suggest that VCM and its metabolites are not retained permanently in liver, because one patient who had been exposed for 12 yr, but not for the last 10 yr, had nearly normal appearing sinusoidal lining cells and Disse's spaces. (13 refs.)

77-4417 **The Chemistry and Biogenesis of the S-containing Metabolites of Vinyl Chloride in Rats.** (Eng.) Green, T. (Imperial Chemical Industries Ltd., Central Toxicology Lab., Alderley Park, Cheshire SK10 4TJ, England); Hathway, D. E. *Chem Biol Interact* 17(2): 137-150; 1977.

The biogenesis of the various urinary S-containing metabolites of vinyl chloride (VC) was investigated in adult male rats. Groups of rats were administered the following chemicals intragastrically: (1) ^{14}C-VC (100 mg/kg; 10 μCi), (2) chloroacetaldehyde (50 mg/kg), (3) S-(2-hydroxyethyl)-L-cysteine (500 mg/kg), or (4) S-(carboxymethyl)-L-cysteine (CMC: 250 mg/kg), and a 24-hr urine sample was taken. Two rats were given repeated daily ip injections of L-(U-^{14}C) cysteine hydrochloride for 5 days and, 30 min after the final injection, a single dose of VC (100 mg/kg/); a 24-hr urine sample was then taken. Two rats were given a single intragastric dose of ^{14}C-VC (450 mg/kg) and sacrificed after 45 min; they were dissected and their livers removed. N-Acetyl-S-(2-hydroxyethyl)cysteine (AHC) was a major VC metabolite, but, according to the method of protective esterification used, either N-acetyl-S-(2-chloroethyl)cysteine or AHC can be isolated from the body fluids. N-Acetyl-S-vinylcysteine was a second related metabolite. These S-containing VC metabolites were not mutagenic in *S. typhimurium*. Administration of the VC metabolites and related compounds to rats indicated that chloroacetaldehyde and CMC, but not chloroacetic acid, are on a pathway connecting VC with thiodiglycollic acid. The fact that chloroacetaldehyde produced both thiodiglycollic acid and AHC in the animal and that CMC was identified among the hydrolytic products from a hepatic extract of VC-treated animals is consistent (1) with the formation of chloroacetaldehyde and (2) with the reaction of chloroethylene oxide or chloroacetaldehyde with glutathione in the presence of a glutathione S-epoxide transferase to give the identified S-containing metabolites. (22 refs.)

77-4418 **Vascular Changes in Vinyl Chloride Workers.** (Dut.) Zielhuis, R. L. (No affiliation given) *Ned Tijdschr Geneeskd* 121(29): 1183-1184; 1977.

A possible method for the early detection of vinyl chloride (VC)- induced abnormalities is discussed. There were changes in the capillaries of the fingers of 55/152 workers who had been exposed to VC for 5-28 yr, but similar changes occurred in only 3/50 controls. The vascular changes consisted of dilated or tortuous vessels and many avascular sites. (8 refs.)

77-4419 **Comparison of the Fate of Vinyl Chloride Following Single and Repeated Exposure in Rats (Meeting Abstract).** (Eng.) Watanabe, P. G. (Toxicology Res. Lab., Dow Chemical Co., Midland, MI); Zempel, J. A.; Gehring, P. J. *Toxicol Appl Pharmacol* 41(1): 174-175; 1977. (no refs.)

77-4420 **The Effect of Vinyl Chloride Monomer, Chloroethylene Oxide and Chloracetaldehyde on DNA Synthesis in Regenerating Rat Liver.** (Eng.) Border, E. A. (Natl. Res. Inst. Occupational Diseases, S. African Medical Res. Council, P O Box 4788, Johannesburg, 2000 S. Africa) Webster, I. *Chem Biol Interact* 17(2): 239-247; 1977.

A study was made of the effects of vinyl chloride monomer (VCM) and two of its presumed metabolites, chloracetaldehyde (CA) and chloroethylene oxide (CEO), on DNA synthesis in the regenerating livers of 100-g Wistar rats subjected to partial hepatectomy. VCM (0.5 ml of a 0.19% solution) injected iv 30 min after partial hepatectomy reduced the first ensuing wave of DNA synthesis (at 21 hr) by about 50%; no effect on the second wave of DNA synthesis (at 30 hr) was evident. Similar treatment with CEO and CA also depressed the first wave of DNA synthesis by about 50%. However, these substances had different effects on the second wave: CEO raised the rate of DNA synthesis by about 50%, but CA tended to desynchronize the normally well-defined second wave. VCM, CEO, and CA, when compared to the reported inhibitory effects of other various carcinogens, have similar effects in retarding DNA replication. (37 refs.)

77-4421 **Carcinogenic Activity of Hexachlorobenzene in Hamsters (Meeting Abstract).** (Eng.) Cabral, J. R. (Eppley Inst. for Res. in Cancer, Univ. Nebraska Medical Center, Omaha, NB); Shubik, P.; Mollner, T.; Raitano, F. *Toxicol Appl Pharmacol* 41(1): 155; 1977. (no refs.)

77-4422 **Effect of Benzene on Hemopoietic Stem Cells.** (Rus.) Frash, V. N. (Inst. Industrial Hygiene and Occupational Diseases, Sverdlovsk, USSR) Iushkov, B. G.; Karaulov, A. V. *Gig Tr Prof Zabol* (12): 44-46; 1976.

In a study designed to evaluate the effect of subacute benzene intoxication on hemopoiesis, lethally irradiated (1,000 R) CBA mice were inoculated with bone marrow cells (10^5) or spleen cells (10^6) from CBA mice treated with benzene (2 ml/kg, every other day, for 4-6 wk). Benzene significantly decreased the number of karyocytes in the bone marrow (7.2/10^6 cells vs 14.5/10^6 cells in controls) and in the spleen (33/10^6 cells vs 389/10^6 cells in controls). The relative effectiveness of colony formation of the bone marrow cells (7.3/10^5) and spleen cells (6.3/10^6) did not differ from control values. In other experiments, colony formation was significantly inhibited in lethally irradiated mice exposed to benzene (2 ml/kg, every other day, for 8 days) and inoculated with 10^5 bone marrow cells (1.2 colonies, compared to 7.3 colonies in controls). Benzene inhibited predominantly the growth of granulocyte and megakaryocyte colonies. (10 refs.)

77-4423 **Mechanism of the Carcinogenic Action of Benzene: Irreversible Binding to Rat Liver DNA.** (Eng.) Lutz, W. K. (Inst. Toxicology, Federal Inst. Technology, CH-8603 Schwerzenbach, Switzerland). *Chem Biol Interact* 18(2): 241-245; 1977.

Inhalation experiments on benzene toxicity in adult male rats indicated that a metabolite of benzene bound to rat liver DNA. Although the identity of this metabolite is unknown, it is thought to be benzene oxide. The alkylating potency o benzene was shown to be about 3,000 times lower than tha of N,N-dimethylnitrosamine. (9 refs.)

77-4424 **Mutagenicity of Methoxyl Derivatives of N-hydroxy-4-aminoazobenzene and 4-Nitroazobenzene.** (Eng.) Hashimoto, Y. (Dept. Hygienic Chemistry, Pharmaceutical Inst., Tohoku Univ., Aobayama, Sendai 980, Japan) Watanabe, H.; Degawa, M. *Gann* 68(3): 373-374; 1977.

The mutagenicity of the 2-methoxyl and 3-methoxyl derivatives of N-hydroxy-4-aminoazobenzene was markedly different in *Salmonella typhimurium*. These findings and studies with 4-nitroazobenzene derivatives indicate a correlation between the mutagenicity of azo dyes and carcinogenicity of the parent dyes. (9 refs.)

77-4425 **Localization of Minor Liver-bound Metabolites of 3′-Methyl-p-dimethylaminoazobenzene with Anti-hapten Antibodies.** (Eng.) Carruthers, C. (Orchard Park Labs., Roswell Park Memorial Inst., Buffalo, NY 14263) Baumler, A.; Neilson, A. *Cancer Res* 37(7): 2099-2104; 1977.

The localization of known and possible metabolites of azocarcinogens, such as p-amino-N,N-dimethylaniline, p-amino-N-monomethylaniline and aniline or aminobenzene, bound to components of liver cells of male Fischer rats fed single or multiple doses of 3′-methyl-p-dimethylaminoazobenzene (3′-Me-DAB) was determined. Antibodies raised against p-azo-N,N-dimethylaniline (p-azo-DA), p-azo-N-monomethylaniline (p-azo-MA), and azo-aniline (azo-B) were used in the indirect fluorescent antibody procedure. Antisera raised against p-azo-N-acetyl-N-methylaniline (p-azo-AMA) were also used, since p-amino-N-acetyl-N-methylaniline (p-amino-AMA) is a possible metabolite of 3′-Me-DAB and it is structurally related to the aniline derivatives examined. Antisera against p-azo-AMA not only reacted in agar with p-azo-AMA-ovalbumin conjugate, but also cross-reacted with p-azo-MA-ovalbumin conjugate. Anti-azo-B and anti-p-azo-MA antisera reacted in agar only with azo-B-ovalbumin and p-azo-MA-ovalbumin conjugates, respectively. The p-azo-DA-ovalbumin conjugate did not react in agar with anti-p-azo-MA, anti-azo-B, or anti-p-azo-AMA antisera. Antisera against p-azo-AMA, azo-B, and p-azo-MA reacted in agar with the cytosol prepared from the livers of rats treated with 3′-Me-DAB or p-amino-AMA. When antisera against p-azo-DA, p-azo-MA, and azo-B were absorbed with cytosol from normal rat liver, these absorbed antisera reacted with liver cells from rats. The antibodies responsible for this reaction were removed from the three antisera by absorption with cytosol from livers of rats fed 3′-Me-DAB, and the antibodies were also removed from the anti-p-azo-MA antisera by absorption with cytosol from the livers of rats fed p-amino- AMA. When anti-p-azo-DA, anti-p-azo-MA, and anti-azo-B antisera were absorbed with the cytosol from normal rat liver, only anti-p-azo-MA antisera reacted with liver cells from rats fed p-amino-AMA; the antibodies responsible for this reaction were removed from the antisera by absorption with cytosol from rats fed p-amino-AMA but not by absorption with cytosol from rats fed 3′-Me-DAB. The antisera raised against p-azo-DA, p-azo-MA, or azo-B did not react with carcinoma cells induced in rat liver by 3′-Me-DAB, but they did react with liver cells adjacent to the carcinomas still capable of binding 3′-Me-DAB. (12 refs.)

77-4426 **Tumors of the Preputial Gland in Rats.** (Eng.) Hiraga, K. (Dept. Toxicology, Tokyo Metropolitan Res. Lab. Public Health, Hyakunincho 3-24-1, Shinjuku-ku, Tokyo 160, Japan) Fujii, T. *Gann* 68(3): 369-370; 1977.

Twelve tumors that developed in the preputial gland of rats administered alkyl benzenesulfonate were examined. There were seven adenomas and five tumors showing squamous metaplasia; other histological findings are summarized. The results suggest that these tumors were not caused by the chemical. (2 refs.)

77-4427 **Effects of Toluene on the Metabolism, Disposition and Hemopoietic Toxicity of [^{3}H]Benzene.** (Eng.) Andrews, L. S. (Dept. Pharmacology, Thomas Jefferson Univ., Philadelphia, PA 19107) Lee, E. W.; Witmer, C. M.; Kocsis, J. J.; Snyder, R. *Biochem Pharmacol* 26(4): 293-300; 1977.

In a study with male Swiss albino (ICR) mice, toluene reduced the level of urinary metabolites of benzene and the benzene-induced inhibition of RBC ^{59}Fe uptake. The data strongly suggest that the metabolism of benzene is closely related to its toxicity. (24 refs.)

77-4428 **Inhibitory Effect of Butylated Hydroxytoluene (BHT) on Intestinal Carcinogenesis in Rats by Azoxymethane.** (Eng.) Weisburger, E. K. (Carcinogen Metabolism and Toxicology Branch, NCI, Bethesda, MD 20014) Evarts, R. P.; Wenk, M. L. *Food Cosmet Toxicol* 15(2): 139-141; 1977.

The administration of butylated hydroxytoluene (BHT) in the diet of male F344 rats concurrently receiving azoxymethane (7.4 mg/kg/wk x 10, sc) resulted in a decreased incidence of intestinal and ear-duct tumors. BHT fed to rats after treatment with azoxymethane had no effect on the incidence of intestinal tumors, although the number of tumors per animal increased slightly. (16 refs.)

77-4429 **Testing of Some Azo Dyes and Their Reduction Products for Mutagenicity Using *Salmonella typhimurium* TA 1538.** (Eng.) Garner, R. C. (Cancer Res. Unit, Univ. York, Heslington, York Y01 5DD, England) Nutman, C. A. *Mutat Res* 44(1): 9-19; 1977.

The following azo dyes were tested for mutagenicity to *Salmonella typhimurium* strain TA1538 using a soft agar overlay method: Naphthol Orange, Sunset Yellow, Amaranth, Carmoisine, Orange G, Sudan Yellow, Ponceau 3R, Ponceau de Xylidine, Sudan 2, and Chrysoidin. Chrysoidin, Sudan Yellow, Ponceau 3R, and Ponceau de Xylidine have been classified as carcinogenic. Various single-ring aromatic amines substituted on the benzene ring were also tested. Sudan 2, Chrysoidin, and a reduction product of Chrysoidin, 1,2,4-triaminobenzene, were mutagenic in the presence of a rat liver activating system. The correlation between mutagenicity and carcinogenicity in this group of compounds is discussed. (23 refs.)

77-4430 **Study of the Possible Carcinogenic Properties of Flexographic Dyes.** (Rus.) Ruchkovskii, B. S. (Inst. Oncological Problems, Acad. Sciences, Ukrainian SSR, USSR) Tiktin, L. A.; Mel'nichenko, A. V.; Dziuba, N. M.; Voitenko, I. N. *Vopr Onkol* 22(10): 88; 1976.

Flexographic dyes, which are used for sealing food packages, may consist of phthalocyanic and azo dyes, titanium white, chimney soot, and other compounds. Chimney soot PM-75, a black dye, was found to contain 0.17 μg/kg benzo(a)pyrene. Mice were given powdered dye daily (0.06% of daily diet) with their food and studied after 3, 10, and 30 days and every 1.5 mo thereafter for 18 mo. In other experiments, dyes dissolved in dimethyl sulfoxide were injected sc into rats in a dose of 50 mg/animal; these rats were observed for 13 mo. Histological and microscopic studies of the organs and tissues showed no cancerous changes in mice or rats. (11 refs.)

77-4431 **Long-Term Studies on Chemically Induced Liver Enlargement in the Rat. III. Structure and Behaviour of the Hepatic Nodular Lesions Induced by Ponceau MX.** (Eng.) Grasso, P. (British Industrial Biological Res. Assoc., Woodmansterne Road, Carshalton, Surrey, England) Gray, T. J. *Toxicology* 7(3): 327-347; 1977.

The pathological effects of Ponceau MX [disodium salt of 1-(2,4-xylylazo)-2-naphthol-3,6-disulfonic acid, 2.5% in the diet] on the livers of female Wistar rats were studied. Liver enlargement occurred after 5-30 wk, followed by cell enlargement, abnormal glycogen deposition, and nodular hyperplasia. After 12 mo of exposure, the appearance of the livers of a group of animals was assessed by laparotomy; these rats were returned to a normal diet for 9 mo and the livers reexamined at autopsy after sacrifice. About half the animals had no nodules at laparotomy, and they were still free of nodules at autopsy. The remainder had nodules ranging in size from 2 to 10 mm in diameter at laparotomy; all of these grew to varying extents so that at autopsy, the diameter ranged from 3 to 30 mm. Histological changes preceded the appearance of hepatic nodules. It is concluded that once established, nodules continue to grow and they either develop fatty degeneration or become malignant. (29 refs.)

77-4432 **Long-Term Studies on Chemically Induced Liver Enlargement in the Rat. II. Transient Induction of Microsomal Enzymes Leading to Liver Damage and Nodular Hyperplasia Produced by Safrole and Ponceau MX.** (Eng.) Crampton, R. F. (British Industrial Biological Res. Assoc., Woodmansterne Road, Carshalton, Surrey, England) Gray, T. J.; Grasso, P.; Parke, D. V. *Toxicology* 7(3): 307-326; 1977.

Sequential biochemical and morphological observations were made of the livers of female Wistar rats fed a diet containing 0.25% safrole or 1% Ponceau MX [disodium salt of 1-(2,4-xylylazo)-2-naphthol-3,6-disulfonic acid] for up to 85 wk. After administration of safrole for 7 days, the relative liver wt was increased about 50% and the activity of various drug-metabolizing enzymes was enhanced by 75%-300%. The continued administration of safrole, however, led to inhibition of drug-metabolizing activity. The liver remained enlarged throughout the administration period; concentrations of cytochrome P-450 reductase, cytochrome b_5, and microsomal protein were elevated. The loss of drug-metabolizing ability was associated with histochemical and ultrastructural evidence of liver damage. The enlarged liver produced by Ponceau MX was initially accompanied by some induction of the drug-metabolizing enzymes, followed by a gradual reversal as treatment continued; histochemical evidence of liver damage was encountered after only 1 wk of treatment. The early cytological changes produced by both compounds were followed by the development of fatty change, cell necrosis, and hepatic nodules. It is suggested that liver enlargement unaccompanied by induction of the drug-metabolizing enzymes may provide an early index of hepatotoxicity. (31 refs.)

77-4433 **Carcinogenic and Mutagenic Activities of Safrole, 1′-Hydroxysafrole, and Some Known or Possible Metabolites.** (Eng.) Wislocki, P. G. (Eppley Inst. Res. Cancer, 42nd Ave. and Dewey Ave., Omaha, NB 68105) Miller, E. C.; Miller, J. A.; McCoy, E. C.; Rosenkranz, H. S. *Cancer Res* 37(6): 1883-1891; 1977.

The carcinogenicity and mutagenicity of metabolites and possible metabolites of safrole and 1′-hydroxysafrole were investigated to assess their importance as possible proximate or ultimate carcinogens. The following species were mutagenic in *Salmonella typhimurium* strains TA1335 and TA100 without metabolic activation: 1′-acetoxysafrole, safrole 2′,3′-oxide, 1′-hydroxysafrole 2′,3′-oxide, 1′-acetoxysafrole 2′,3′-oxide, and 1′-oxosafrole 2′,3′-oxide. The following species we not mutagenic either in the presence or absence of standard rat liver activating system: safrole, isosafrol 2′,3′-dihydrosafrole, 1′-hydroxysafrole, 3′hydroxyis safrole, 3′-acetoxyisosafrole, and 1-oxosafrole. Multipl topical applications to mice of 1′-hydroxy 2′,3′-oxid followed by repetitive doses of croton oil, formed skin papillomas in 10/30 mice. Under the same conditions, the following agents did not induce a significant number of these tumors: safrole, 1′-acetoxysafrole, 1′-hydroxysafrole, 1′ oxosafrole, safrole 2′,3′-oxide, or 1′-acetoxy 2′,3′-oxide. Other routes of administration were also investigated. It is concluded that multiple electrophiles, particularly safrole 1′ sulfate, 1′-hydroxy 2′,3′-oxide, 1′-oxosafrole, and safrol 2′,3′-oxide, must be considered possible ultimate ca cinogenic metabolites of safrole in mice and rats. (3 refs.)

77-4434 **Long-term Toxicity Study with Orthotoluenesulfonamide and Saccharin (Meetin Abstract).** (Eng) Arnold, D. L. (Toxicology Res. Div., Bureau Chemical Safety, Health Protection Branch, Ottawa Ontario, Canada); Charbonneau, S. M.; Moodie, C. A. Munro, I. C. *Toxicol Appl Pharmacol* 41(1): 164; 1977 (1 ref.)

77-4435 **Six-year Study of Saccharin in Rhesus Monkeys (Meeting Abstract).** (Eng) McChesney, E W. (Inst. Comparative and Human Toxicology, Alban Medical Coll., Albany, NY); Coulston, F.; Benitz, K. F. *Toxicol Appl Pharmacol* 41(1): 164; 1977.

77-4436 **Eight-year Study of Cyclamate in Rhesus Monkeys (Meeting Abstract).** (Eng) Coulston, F. (Inst. Comparative and Human Toxicology, Albany Medical Coll., Albany NY); McChesney, E. W.; Benitz, K. F. *Toxico Appl Pharmacol* 41(1): 164-165; 1977. (no refs.)

77-4437 **Three Cases of Human Bladder Cancer Following High Dose Cyclamate Ingestion.** (Eng.) Barkin, M. (Div. Urology, Sunnybrook Medical Center, 2075 Bayview Ave., Toronto, Canada) Comisarow, R. H.; Taranger, L. A.; Canada, A. *J Urol* 118(2): 258-259; 1977.

Three men, aged 66, 49, and 64 yr, each developed transitional cell carcinoma of the bladder after ingestion of large quantities of cyclamate over a long period of time. It is suggested that bladder cancer patients be questioned about their intake of cyclamates. (17 refs.)

77-4438 **Asbestosis, Hyalin Pleural Plaques, Pleural Mesothelioma.** (Ger.) Sieber, R. (Institut fur klinische Radiologie und Institut fur Pathologie der Universitat Basel, Basel, Switzerland) Elke, M.; Dalquen, P. *Praxis* 66(26): 798-803; 1977.

The case report of a 72-yr-old man who developed malignant pleural mesothelioma of the right lung is presented. He had a 41-yr history of exposure to asbestos. Various aspects of the diagnosis are discussed. (22 refs.)

77-4439 **Asbestos Exposure and Laryngeal Carcinoma.** (Eng.) Freifeld, S. (392 Springfield Ave., Summit, NJ 07901) *JAMA* 238(12): 1280; 1977.

The case history of a 63-yr-old man who developed laryngeal carcinoma is presented. He had worked for 30 yr in an asbestos processing plant. He had no history of other factors that could have contributed to the carcinoma. (3 refs.)

77-4440 **Fate of Methyl Methacrylate in Rats.** (Eng.) Bratt, H. (Imperial Chemical Industries, Central Toxicology Lab., Alderley Park, Cheshire, SK10 4TJ, England) Hathway, D. E. *Br J Cancer* 36(1): 114-119; 1977.

Since up to 88% of labeled methyl methacrylate is expired from the rat lung as CO_2, a previous report of its teratogenic effects resulting from ip injection are questioned. The pathways involved are unlikely to yield any harmful metabolites. Furthermore, teratogens may be absorbed from the peritoneal cavity but not via the placenta. (7 refs.)

77-4441 **THPOH-NH_3 FR Cotton: Results of the Ames Test (Letter to Editor).** (Eng.) Mazzeno, L. W. (Southern Regional Res. Center, U.S. Dept. Agriculture, New Orleans, LA) Gruener, N. *Textile Chemist Colorist* 9(8): 38; 1977.

Results of the Ames test for the mutagenicity of THPOH-NH_3 polymer and THPOH-NH_3-treated fabrics showed no systematic increases in revertants, even with increases in THPOH-NH_3 concentration. (1 ref.)

77-4442 **Mutagenicity Testing of Styrene and Styrene Epoxide in *Salmonella typhimurium.*** (Eng.) Stoltz, D. R. (Toxicology Res. Div., Food Res. Labs., Health Protection Branch, Tunney's Pasture, Ottawa K1A OL2, Canada) Withey, R. J. *Bull Environ Contam Toxicol* 17(6): 739-742; 1977.

The mutagenicity of styrene and styrene epoxide (both dissolved in ethanol and subsequently diluted to 20% with water) was examined in spot tests and plate incorporation assays using various strains of *Salmonella typhimurium.* At concentrations up to 1 mg per plate, styrene was not mutagenic, even in the presence of liver metabolizing systems. The epoxide, which is a metabolite of styrene, was specifically mutagenic for strains TA1535 and TA1000, indicating that the epoxide acts as a base-substitution mutagen. Poor conversion to the epoxide and efficient removal of the epoxide by liver enzymes may contribute to the lack of demonstrable mutagenic activity of styrene. Without more specific data on the human metabolism of styrene, the potential carcinogenic threat of environmental styrene is impossible to estimate. (10 refs.)

77-4443 **Testicular Leydig Cells and Δ^5-3β-Hydroxysteroid Dehydrogenase in Cadmium-treated Toads (*Bufo melanostictus*).** (Eng.) Biswas, N. M. (Dept. Physiology, Univ. Coll. Science, 92 Acharya Prafullachandra Road, Calcutta 700009, India) Chanda, S.; Ghosh, A. *Experientia* 33(2): 277-278; 1977.

The injection of cadmium chloride into male *Bufo melanostictus* toads resulted in increased Leydig cell size and Δ^5-3β-hydroxysteroid dehydrogenase activity in the testis. It is suggested that the chemical stimulates the cell's activity by increasing gonadotropin synthesis. (14 refs.)

77-4444 **Cadmium and Prostatic Carcinoma (Letter to Editor).** (Eng.) Kolonel, L. (Epidemiology and Demography Program, Cancer Center, Univ. Hawaii, Honolulu, HI 06822) Winkelstein, W. *Lancet* 2(8037): 566-567; 1977.

The relationship between cadmium and prostatic carcinoma was investigated in 176 prostatic carcinoma cases and 269 controls. An increased risk was noted only in individuals with occupational exposure, but these values were not statistically significant. There was no synergistic effect between occupational exposure and cigarette smoking. (9 refs.)

77-4445 **Effect of Chronic Oral Cadmium Exposure and Withdrawal on Cadmium Residues in Organs of Mice.** (Eng.) Exon, J. H. (Sch. Veterinary Medicine, Oregon State Univ., Corvallis, OR 97331) Lamberton, J. G.; Koller, L. D. *Bull Environ Contam Toxicol* 18(1): 74-76; 1977.

The effects of chronic po cadmium exposure on the kidney and liver, and the residues of the element in these organs after withdrawal, were examined in SW/Sim mice. The biological half life in the liver was approx 180 days; an estimation of the half life in the kidney was not made because of the stability of cadmium in that organ. (8 refs.)

77-4446 **Chronic Oral Toxicity of Beryllium in the Rat (Meeting Abstract).** (Eng.) Morgareidge, K. (Food and Drug Res. Lab., Inc., East Orange, NJ); Cox, G. E.; Bailey, D. E.; Gallo, M. A. *Toxicol Appl Pharmacol* 41(1): 204-205; 1977. (no refs.)

77-4447 **Chromosomal Aberrations and Morphological Transformation in Hamster Embryonic Cells Treated with Potassium Dichromate In Vitro.** (Eng.) Tsuda, H. (Section Cell Biology and Cytogenetics, Biological Res. Center, Central Res. Inst., Japan Tobacco and Salt Public Corporation, Hatano, Kanagawa-ken 257, Japan) Kato, K. *Mutat Res* 46(2): 87-94; 1977.

Treatment of hamster embryonic cells with potassium dichromate (0.1-0.5 μg/ml culture) for 24 hr resulted in consistent chromosomal aberrations. This effect was lessened by adding a reducing agent, $NaSO_3$. Divalent and trivalent chromium salts were ineffective in increasing chromosomal aberrations, but CrO_3 was highly effective. Apparently, only hexavalent compounds exert powerful biological effects. (13 refs.)

77-4448 **Fetal Toxicity and Transplacental Transport of Ni(II) in Rats (Meeting Abstract).** (Eng.) Sunderman, F. W. (Univ. Connecticut Sch. Medicine, Farmington, CT); Shen, S.; Mitchell, J.; Allpass, P.; Damjanov, I. *Toxicol Appl Pharmacol* 41(1): 205; 1977. (no refs.)

77-4449 **Ultrastructural Morphometric and Biochemical Studies of Chronic Arsenic Exposure on Hepatocyte Mitochondria of Rats and Mice (Meeting Abstract).** (Eng.) Fowler, B. A. (Environmental Toxicology Branch, Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC); Woods, J. S.; Schiller, C. M. *Toxicol Appl Pharmacol* 41(1): 145; 1977. (no refs.)

77-4450 **Placental Permeability of Arsenate Ion During Early Embryogenesis in the Hamster.** (Eng.) Hanlon, D. P. (Dept. Microbiology and Biochemistry, Coll. Agriculture, Univ. Vermont, Burlington, VT 05401); Ferm, V. H. *Experientia* 33(9): 1221-1222; 1977.

Studies with pregnant hamsters indicated that the arsenate ion (^{74}As) crosses the placental barrier on the 8th day of embryogenesis, a critical time in organogenesis, and then acts as a teratogen. The findings support the concept that arsenate acts specifically on the cephalic mesenchyme of the embryo. (6 refs.)

77-4451 **Chronic Inhalation of Cobalt Oxide and Cigarette Smoke by Hamsters.** (Eng.) Wehner, A. P. (Biology Dept., Battelle Pacific Northwest Lab., Richland, WA) Busch, R. H.; Olson, R. J.; Craig, D. K. *Am Ind Hyg Assoc J* 38(7): 338-346; 1977.

Although whole-body exposure of hamsters to an aerosol of cobalt oxide resulted in pneumoconiosis, no tumorigenic effect was observed. Animals exposed to cigarette smoke had a significant increase in the number of lung tumors, but they also had a longer life span. The latter could account for the increased tumor incidence. (29 refs.)

77-4452 **Studies on the Effect of Chronic Cigarette Smoke Inhalation in Syrian Golden Hamsters and the Importance of Vitamin A on Morphological Alterations After Smoke Exposure.** (Ger.) Dontenwill, W. (Agathe-Lasch-Weg 25, D-2000 Hamburg 52, W. Germany) Chevalier, H. J.; Harke, H. P.; Klimisch, H. J.; Kuhnigk, C.; Reckzeh, G.; Schneider, B. *Z Krebsforsch* 89(2): 153-180; 1977.

Chronic inhalation of cigarette smoke from reference cigarettes and modified cigarettes induced different stages of leukoplakias and carcinomas in the larynx of Syrian golden hamsters. The incidence and intensity of alterations were distinctly dose- and time-dependent; moreover, they were dependent on cigarette type or tar content. Laryngeal changes were less severe in the group exposed to smoke from cigarettes with a low tar content. Modified cigarettes were made from 50% of the tobacco mixture from reference cigarettes and 50% of puffed tobacco, tobacco sheets, or new smoking material. Smoke exposure reduced body wt and increased inflammations of the nasal and oral cavity, the number of ptyaloliths, and the incidence of "smoke cells" in the lung. The number of spontaneous tumors and changes in the liver, spleen, kidney, and adrenal glands, as well as vascular diseases, were not dependent on treatment. Additional chronic treatment with vitamin A induced a considerable increase in laryngeal papillary leukoplakias and a distinct decrease in verrucous leukoplakias. An increased incidence of carcinomas was not observed. Animals treated with vitamin A and smoke developed a higher number of tumors in the thyroid gland. Survival time was reduced. Animals treated with vitamin A only showed an increase in dysplasias and carcinomas of the digestive tract. (39 refs.)

77-4453 **Mutagenicity of Smoke Condensate from Cigarettes, Cigars and Pipe Tobacco.** (Eng.) Sato, S. (Biochemistry Div., Natl. Cancer Center Res. Inst., Tsukiji, Chuo-ku, Tokyo 104, Japan) Seino, Y.; Ohka, T.; Yahagi, T.; Nagao, M.; Matsushima, T.; Sugimura, T. *Cancer Lett* 3(1/2): 1-8; 1977.

Smoke condensates from cigarettes, cigars, and pipe tobacco were mutagenic for *Salmonella typhimurium* TA100 and

TA98 when activated by a rat liver microsomal system. The mutagenicity of a unit wt of smoke condensate was high in cigars, low in pipe tobacco, and intermediate in cigarettes. Specific mutagenic activity was almost comparable among smoke condensates from low- to high-tar cigarettes, although some variations were observed among American, European, and Japanese brands. The marked mutagenicity of cigarette smoke condensate could not be explained by the benzo(a)pyrene or nitroso compounds it contained, suggesting the presence of other potent mutagens in tobacco smoke condensates. (23 refs.)

77-4454 **Factors Affecting Mutagenic Activity of Cigarette Smoke Condensate in *Salmonella typhimurium* TA 1538.** (Eng.) Mizusaki, S. (Central Res. Inst., Japan Tobacco and Salt Public Corporation, 6-2 Umegaoka, Midori-ku, Yokohama, Kanagawa 227, Japan) Takashima, T.; Tomaru, K. *Mutat Res* 48(1): 29-36; 1977.

Smoke condensates from Burley tobacco, flue-cured tobacco, and various brands of commercial cigarettes were tested for mutagenicity in a microsomal test system with *Salmonella typhimurium* TA1538. Smoke condensate from Burley tobacco had a much higher mutagenic activity than that from tobacco. Increased mutagenicity was observed with smoke condensates from Burley tobacco grown with increasing amounts of nitrogen fertilizer, and from commercial cigarettes blended with Burley tobacco. There was a significant correlation between the nitrate content of a cigarette and the mutagenicity of the resulting smoke condensate. The results suggest that the nitrate in cigarettes may influence the formation of potential mutagens during the smoking of a cigarette. (15 refs.)

77-4455 **Dissociation of Increases in Levels of 3′:5′-Cyclic AMP and 3′:5′-Cyclic GMP from Induction of Ornithine Decarboxylase by the Tumor Promoter 12-O-Tetradecanoyl Phorbol-13-acetate in Mouse Epidermis In Vivo.** (Eng.) Mufson, R. A. (McArdle Lab. Cancer Res., Univ. Wisconsin Medical Center, Madison, WI 53706) Astrup, E. G.; Simsiman, R. C.; Boutwell, R. K. *Proc Natl Acad Sci USA* 74(2): 657-661; 1977.

A single topical application of 17 nanomoles (nmol) of 12-O-tetradecanoyl phorbol-13-acetate (TPA) caused a marked (200-400 fold) induction of ornithine decarboxylase activity in epidermal and epidermal-dermal preparations from female Charles River mice. No change in the basal level of cyclic AMP occurred in epidermal-dermal preparations within 30 min of TPA application. Ip injection of the β-agonist isoproterenol (0-300 nmol) resulted in a dose-dependent accumulation of cyclic AMP 10 min after injection, but had no effect on ornithine decarboxylase induction. When isoproterenol was injected 10 min prior to an application of either 1.7 or 17 nmol of TPA, the magnitude of the ornithine decarboxylase induction was the same as induction with TPA alone. Topical application of 17 nmol of TPA did not increase the level of cyclic guanosine monophosphate (GMP) present in the mouse epidermal-dermal preparations 2-20 min after application. Ip injection of 1.75 µmol of dibutyryl cyclic GMP caused a sixfold increase in the level of cyclic GMP and/or butyryl derivatives of cyclic GMP in epidermal-dermal preparations within 5 min of injection, and the level remained elevated for at least 20-30 min. This dose of dibutyryl cyclic GMP was incapable of inducing ornithine decarboxylase. Injection of dibutyryl cyclic GMP 5 min after application of 1.7 nmol of TPA or 30 min before application of 17 nmol of TPA did not alter the magnitude of the ornithine decarboxylase induction produced by TPA alone. These results suggest that early increases in the total intracellular levels of either cyclic AMP or cyclic GMP are not part of the mechanism by which TPA induces ornithine decarboxylase in the epidermis. (34 refs.)

77-4456 **Effect of Serum Level on the Proliferative Response of Epidermal Cells to 12-O-Tetradecanoyl-Phorbol-13-Acetate (TPA) (Meeting Abstract).** (Eng.) Hennings, H. (NIH, Bethesda, MD 20014) Michael, D. *Proc Am Assoc Cancer Res* 18: 66; 1977. (no refs.)

77-4457 **Screening Procedure for Phorbol Esters Using Brine Shrimp (*Artemia salina*) Larvae (Letter to Editor).** (Eng.) Kinghorn, A. D. (Dept. Pharmacognosy, Sch. Pharmacy, Univ. Mississippi, University, MS 38677) Harjes, K. K.; Doorenbos, N. J. *J Pharm Sci* 66(9): 1362-1363; 1977.

Brine shrimp (*Artemia salina*) larvae have been found to be selectively toxic to phorbol esters of different cocarcinogenic potencies and also to be sensitive when compared with the pesticides rotenone and picrotoxin. The inexpensive testing method can be performed by persons with little biological training. The screening procedure is described and test results are presented for various compounds. (8 refs.)

77-4458 **Tumor Promoters Inhibit Spontaneous Differentiation of Friend Erythroleukemia Cells in Culture.** (Eng.) Rovera, G. (Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA 19104) O'Brien, T. G.; Diamond, L. *Proc Natl Acad Sci USA* 74(7): 2894-2898; 1977.

In a search for factors that might affect spontaneous differentiation, diesters of the diterpene alcohol, phorbol, which have a wide range of tumor-promoting activity on mouse skin, were tested with three spontaneously differentiating clones (D7, D7/1, and D7/64) of Friend erythroleukemia cells. These cells are characterized by the presence of 40%-70%

benzidine-positive cells synthesizing Hb in the absence of inducing drugs. They were treated with 1.6×10^{-4} M phorbol, 12-O-tetradecanoyl-phorbol-13-acetate (TPA), 4-α-phorbol-12,13-didecanoate (4-α-PDD), phorbol-12,13-dibenzoate (PDB), phorbol-12,13-diacetate (PDA), and phorbol-12,13-didecanoate (PDD). TPA and PDD were the most active, PDB less active, and PDA, 4-α-PDD, and phorbol were inactive in inhibiting spontaneous erythroid differentiation in culture. The results correlated with the tumor-promoting activity of these diesters on mouse skin. Most striking was the difference in activity between PDD and the epimer 4-α-PDD. Inhibition by TPA was max after 4 days of treatment and it was reversible, no matter how long the treatment. After removal of the compound, TPA-treated cells retained their potential for producing a high percentage of spontaneously differentiating cells, unlike control cells, which gradually reverted to a population with a low percentage of benzidine-positive cells. Tumor promoters probably act in vivo by interfering with normal cell differentiation. (26 refs.)

77-4459 **Physiological Effects of Trace Elements and Chemicals in Water.** (Eng.) Varma, M. M. (Bio-Environmental Engineering and Sciences, Howard Univ., Washington, DC) Serdahely, S. G.; Katz, H. M. *J Environ Health* 39(2): 90-101; 1976.

The physiological effects of trace amounts of water pollutants are discussed. Although mercury, cadmium, lead, beryllium, chromium, manganese, and fluoride are all toxic to humans, they have not been implicated in human carcinogenesis. Tumors have been induced in rat kidneys following chronic administration of lead in their drinking water. There is a correlation between a high incidence of skin cancer and high arsenic levels in drinking water. The consumption by infants of water with a high nitrate concentration may result in the production of nitrosamines, which can lead to stomach cancer. Many organic residues found in water have been linked to cancer in animals and/or humans. Polychlorinated biphenyls induced bladder cancer in rats. Commercial 1-naphthylamine contains up to 10% 2-naphthylamine, a known carcinogen. N-nitroso compounds are highly carcinogenic, and they also induce chromosomal breaks and aberrations. Urethane and certain other carbamates cause mutation, chromosome breaks, teratogenic effects, and cancer in test organisms. Of the 66 chemicals whose concentrations have been measured in water, 15/33 examined were carcinogenic in one or more animal tests. Of 430 potential pollutants, 17/87 examined were carcinogenic. (61 refs.)

77-4460 **The Occurrence of Caffeine in the Air of New York City.** (Eng.) Dong, M. (American Health Foundation, Naylor Dana Inst. for Disease Prevention, Valhalla, NY 10595) Hoffmann, D.; Locke, D. C.; Ferrand, E. *Atmos Environ* 11(7): 651-653; 1977.

In a study conducted between January and April of 1975, caffeine was found to be a major constituent of the particulate organic matter (POM) in New York City air. This finding is significant because the carcinogenicity of POM, which contains polynuclear aromatic hydrocarbons and aza-arenes, can be modified by the presence of caffeine. Coffee roasting plants in the city and in nearby New Jersey may explain the abundance of atmospheric caffeine. (8 refs.)

77-4461 **Primary Hepatocyte Cultures for the Investigation of the Fate and Mechanism of Action of Environmental Chemicals (Meeting Abstract).** (Eng.) Dougherty, K. K. (Dept. Environmental Toxicology, Univ. California, Davis, CA 95616); Spilman, S. D.; Green, C. E.; Steward, A. R.; Byard, J. L. *Toxicol Appl Pharmacol* 41(1): 190; 1977. (no refs.)

77-4462 **Testing the Mutagenic Potency of Chemical Substances in a Linear Host-mediated Assay (LIHMA). Part II. Comparison with the Conventional Host-mediated Assay and Statistical Evaluation of the Data.** (Eng.) Lorenz, R. J. (Bundesforschungsanstalt fur Viruskrankheiten der Tiere in Tubingen, P. O. Box 1149, D-7400 Tubingen, W. Germany) Vollmar, J.; Grafe, A. *Mutat Res* 44(3): 327-336; 1977.

A linear host-mediated assay that measures not only the mutagenic potential of a compound but also any additional antibacterial potency is presented. This assay thus avoids misclassification due to interference of undetected antibacterial activity. Regression analysis allows calculation of the sensitivity and reliability of the assay. (4 refs.)

77-4463 **In Vivo-In Vitro Studies with Tracheal Epithelium for Early Detection of Transformation (Meeting Abstract).** (Eng.) Terzaghi, P. (ORNL, Oak Ridge, TN 37830) Yarita, T.; Williams, M. L.; Griesemer, R. A.; Nettesheim, P. *Proc Am Assoc Cancer Res* 18: 106; 1977. (no refs.)

See also:

* (Rev.): 77-4201, 77-4204, 77-4205, 77-4206, 77-4207, 77-4208, 77-4209, 77-4210, 77-4211, 77-4212, 77-4213, 77-4214, 77-4215, 77-4216, 77-4217, 77-4218, 77-4219, 77-4220, 77-4221, 77-4222, 77-4223, 77-4224, 77-4225, 77-4226, 77-4227, 77-4241, 77-4250, 77-4251, 77-4252, 77-4253, 77-4254.
* (Phys.): 77-4472, 77-4486, 77-4487, 77-4488.
* (Immun.): 77-4554, 77-4556, 77-4557, 77-4559, 77-4563, 77-4565, 77-4570, 77-4580, 77-4587.
* (Path.): 77-4620, 77-4634, 77-4643, 77-4685, 77-4694, 77-4698.
* (Epid.-Biom.): 77-4705, 77-4708, 77-4710, 77-4711, 77-4712, 77-4715, 77-4718, 77-4723, 77-4724.

7-4464 **Microwave Radiation Not Known To Be Teratogenic.** (Eng.) Wheater, R. H. (AMA Dept. Environmental, Public, and Occupational Health, Chicago, IL) Howen, G. G. *JAMA* 238(8): 895; 1977.

Studies have indicated that the only effect of microwave adiation on the human reproductive system is a temporary and reversible reduction in testicular function. Teratogenic abnormalities noted in lower animals have only occurred at doses superior to those resulting from microwave oven exposure. (1 ref.)

77-4465 **A Theory of the Induction of Bone Cancer by Alpha Radiation.** (Eng.) Marshall, J. H. (Center Human Radiobiology, Argonne Natl. Lab., Argonne, IL 60439) Groer, P. G. *Radiat Res* 71(1): 149-192; 1977.

A theory for the induction of osteosarcoma by α particles was constructed that fits the data for radium in man and dog over the entire dose-time-response surface. The theory is summarized as follows: an endosteal cell is initiated twice by α radiation at a certain dose rate, which is any function of time. It is then promoted by tissue remodeling to become the first cell of an osteosarcoma. Cells killed at any stage are replaced by stem cells. The rate of killing is approx 10^5 times larger than the rate of initiation. The osteosarcoma cell multiplies to become an observable tumor in 2-3 yr in dog or 3-6 yr in man. The essence of the theory is that two α particles transform an endosteal cell into a dormant malignant cell, but that α radiation does not cause that cell to multiply to become a bone tumor. The five sections of the paper include: (1) a new method of three-dimensional analysis that provides a firm basis for the development and fitting of theoretical models and derives more information than previous methods from the data for internal emitters; (2) statistical methods to fit the three-dimensional models to the data; (3) development of the theory from physiological considerations, description of the mechanisms affecting endosteal cells, and introduction of parameters for the equations; (4) four differential equations and their solutions; (5) nonmathematical summary of the theory, its results, and its predictions. (54 refs.)

77-4466 **Mathematical Models of Age and Ultraviolet Effects on the Incidence of Skin Cancer Among Whites in the United States.** (Eng.) Fears, T. R. (Field Studies and Statistics Program, NCI 7910 Woodmont Ave., Bethesda, MD 20014) Scotto, J.; Schneiderman, M. A. *Am J Epidemiol* 105(5): 420-427; 1977.

The relationship between short-wavelength UV radiation and skin cancer was studied using a mathematical model and cancer incidence data from Dallas-Fort Worth, Minneapolis-St. Paul, San Francisco-Oakland, and Iowa. A simple power relationship provided a good description of UV-skin cancer incidence relationships. The form of this power function suggested that the risk of nonmelanoma skin cancer is related to cumulative lifetime UV exposure and that the risk of melanoma skin cancer is related to annual UV exposure. However, the actual incidence rates also depended on location-specific demographic and environmental variables other than UV radiation. (12 refs.)

77-4467 **Skin Cancer: Comparison of Aggressive Potentials of Sunlight-induced and X-Ray-induced Tumors.** (Eng.) Spoor, H. J. (568 Park Ave., New York, NY 10021) Lindo, S. D.; Erlandson, R. A. *Cutis* 20(1): 74-80; 1977.

Data on all cases of skin cancer seen in a private practice in New York City between 1950 and 1975 were reviewed to determine the differences in clinical behavior between sunlight- and x-ray-induced forms. Ultrastructural features were also compared. There were 361 single-lesion cases (11 x-ray-induced) and 189 multiple-lesion cases (41 x-ray-induced). The group with lesions induced by x-ray had a conversion rate (from single to multiple) of 64%, compared with 15% in the sun-exposed group. Basal cell carcinoma (BCC) was the most common skin cancer in all groups, but it was more dominant as the initial lesion in the x-ray group. In patients with multiple lesions, BCC was also dominant in subsequent lesions, but it occurred with greatest frequency in the x-ray group. Lesions induced by x-ray occurred in greater numbers (av 7.38 vs 2.89) and more often (0.81/yr vs 0.35/yr) than those induced by sun. Recurrences were also greater in the x-ray group (20% vs 5%). Aggressive behavior of BCC to the extent of bone invasion was seen only once, in a lesion caused by x-ray epilation. Under the electron microscope, x-ray-induced BCC showed more anaplastic features than the sun-induced or nevoid varieties. The former showed greater loss of polarity, more variation in size and shape, greater nuclear and nucleolar atypia, more marked focal dyskeratosis, increased numbers of mitotic cells, and more basal lamina discontinuities. (10 refs.)

77-4468 **The Shape of the Ultraviolet Inactivation Curve for Transforming DNA.** (Eng.) Setlow, J. K. (Biology Dept., Brookhaven Natl. Lab., Upton, Long Island, NY 11973) *Nature* 268(5616): 169-170; 1977.

When a cell receiving UV irradiation lacks both excision and postreplication repair, the UV inactivation curve for transforming DNA is a simple exponential relation. The previously observed inverse square relation results from the repair processes themselves, rather than from recombination between irradiated transforming DNA and recipient DNA. (23 refs.)

77-4469 **Excision Repair and DNA Synthesis after Ultraviolet Light Exposure in African Green Monkey Kidney CV-1 Cells and Simian Virus 40 (SV40) (Meeting Abstract).** (Eng.) Williams, J. I. (Univ. California, San Francisco, CA) *Diss Abstr Int [B]* 38(2): 539; 1977. (no refs.)

77-4470 **The Recovery of Normal DNA Replication Kinetics in Ultraviolet-irradiated Chinese Hamster Cells.** (Eng.) Meyn, R. E. (Dept. Physics, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX 77030) Kasschau, M. R.; Hewitt, R. R. *Mutat Res* 44(1): 129-138; 1977.

The rate of DNA replication in synchronized Chinese hamster ovary cells was analyzed during the second S phase following UV irradiation. The cells were synchronized by treating mitotic cells with hydroxyurea for 9 hr. After UV irradiation (5 joules/m^2), the cells were allowed to progress until the next mitosis, when they were resynchronized at the beginning of the second S phase. The DNA replication rate was determined by measuring the proportion of DNA that achieved hybrid buoyant density on CsCl density gradients as a function of incubation time with 5-bromodeoxyuridine. UV irradiation depressed the DNA replication rate to about 70% of the rate in unirradiated control cells during the first S phase. In contrast, when the irradiated cells were allowed to progress to mitosis and were resynchronized at the beginning of the second S phase, the DNA replication kinetics were identical to those of unirradiated controls. This shows that the cells have recovered completely from the irradiation-induced inhibition of DNA synthesis by the time they enter their second S phase. (32 refs.)

77-4471 **Hyperthermic Effects on DNA Repair (Meeting Abstract).** (Eng.) Corry, P. M. (M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX 77030) Robinson, S.; Getz, S. *Phys Med Biol* 22(1): 146; 1977. (no refs.)

77-4472 **Interactions of Caffeine with the DNA of Chinese Hamster Cells.** (Eng.) Tondeur, F (Laboratoire de Biophysique et Radiobiologie, Universit Libre de Bruxelles, rue des Chevaux 67, B 1640 Rhode St Genese, Belgium) Rommelaere, J. *Biochim Biophys Act* 474(4): 562-570; 1977.

Interactions between caffeine and DNA were studied in cultured hamster V79 cells. Incubation of V79 cells with ^{3}H caffeine (10 μCi/m) resulted in the transfer of radioactivit to DNA. This occurred during the S phase of the cell cycl and involved parenteral as well as newly synthesized strands The replacement of thymidine by bromodeoxyuridin (BUdR) prevented the incorporation of caffeine radioactivit into the DNA strand containing BUdR. Thymine was th only base that became labeled, and the methyl groups of caffeine appeared to participate in the biosynthesis of thymine. UV irradiation increased the association of radioactivity from caffeine with DNA. A direct interaction of caffeine with secondary UV-induced DNA lesions could be responsible fo the radiosensitizing effect of the drug; ie, the inhibition o postreplication repair in eukaryotic cells. (31 refs.)

77-4473 **Enhanced Antibody Affinity in Sublethally Irradiated Mice and Bone Marrow Chimeras.** (Eng.) Doria, G. (CNEN-Euratom Immunogenetics Group, Lab. Radiopathology, C.S.N. Casaccia, Rome, Italy) Gorini, G.; Di Michele, A. *Proc Natl Acad Sci USA* 74(2): 707-710; 1977.

Sublethally irradiated C3HeB/FeJ and DBA/2J mice primed with dinitrophenyl (Dnp)-keyhole limpet hemocyanin immediately after irradiation (450 R) or 30 days later and subsequently boosted with a second injection of antigen displayed a secondary response to Dnp characterized by antibody affinity greater than that in unirradiated controls. Also, in radiation chimeras primed with Dnp-keyhole limpet hemocyanin 120 days after syngeneic or allogeneic bone marrow transplantation, the Dnp antibodies produced after boosting were of higher affinity than the antibodies raised in normal mice. These findings are tentatively attributed to lack of suppressor T lymphocytes in sublethally irradiated mice and bone marrow chimeras, in whom the enhanced ability to produce antibodies of high affinity may compensate for quantitative defects of the immune system. (23 refs.)

77-4474 **Post-irradiation Pituitary Sarcoma.** (Eng.) Powell, H. C. (Dept. Pathology, Univ. California, San Diego, La Jolla, CA 92093) Marshall, L. F.; Ignelzi, R. J. *Acta Neuropathol (Berl)* 39(2): 165-167; 1977.

A report is presented of a 65-yr-old man who developed a

ituitary sarcoma 13 yr after being irradiated with 5,000 rads
f cobalt irradiation for a pituitary adenoma. The tumor lay
n the path of the irradiation, did not metastasize, and con-
ained benign-appearing pituitary adenoma interspersed with
he spindle cell tumor. (12 refs.)

77-4475 **Radiation Risks with Diagnostic X-Rays.** (Eng.) Gregg, E. C. (Dept. Radiology, Case Western Reserve Univ., Cleveland, OH 44106) *Radiology* 123(2): 447-453; 1977.

Calculations are given that correlate the risk of carcinogenesis with various diagnostic radiological procedures. There is a relatively large number of examinations that can be allowed for most of the diagnostic procedures except mammography in women aged 20-34 and computerized tomography scans of the skull. (24 refs.)

77-4476 **Breast Cancer Following X-ray Therapy for Acute Postpartum Mastitis (Meeting Abstract).** (Eng.) Shore, R. (New York Univ. Medical Center, New York, NY 10016) Hempelmann, L.; Pasternack, B.; Kowaluk, E. *Am J Epidemiol* 106(3): 230; 1977. (no refs.)

77-4477 **Radiation-induced Bladder Tumors.** (Eng.) Duncan, R. E. (Div. Urology, Univ. Cincinnati Medical Center, Cincinnati, OH) Bennett, D. W.; Evans, A. T.; Aron, B. S.; Schellhas, H. F. *J Urol* 118(1/part 1): 43-45; 1977.

The incidence of bladder tumors in 2,674 women who received radiation for treatment of carcinoma of the uterine cervix was 57.6 times that of the general population. The neoplasms became evident 6 mo to 20 yr after radiotherapy. (21 refs.)

77-4478 **Undifferentiated Sarcoma. Arising in Previous Hodgkin's Radiation Field.** (Eng.) Jochimsen, P. R. (Dept. Surgery, Univ. Iowa Hosp. and Clinics, Iowa City, IA 52242) *JAMA* 238(13): 1396-1397; 1977.

The case report of a 49-yr-old woman who developed undifferentiated sarcoma of the chest wall 8 yr after chest irradiation for Hodgkin's disease is presented. This conforms to the mean latency period of 10.2 yr between irradiation and development of sarcoma. (5 refs.)

77-4479 **Erythroleukemia (Di Guglielmo's Disease). Occurrence 28 Years after Thorium Administration.** (Eng.) Waddell, C. C. (Hematology Section, Medical Service, Veterans Admin. Hosp., 2002 Holcombe Blvd., Houston, TX 77211) Brown, J. A.; Rueb, D. L. *JAMA* 238(5): 423; 1977.

A 56-yr-old man developed erythroleukemia 28 yr after he had received an iv injection of thorium dioxide (Thorotrast). He died 9 mo after the diagnosis was established. (3 refs.)

77-4480 **Pronounced Deficiency in T-Cells and Lymphocyte Chromosomal Aberrations in a Patient with Sarcoidosis, Myelofibrosis and Acute Leukemia Following Thorotrast Angiography.** (Eng.) Brandt, L. (Dept. Internal Medicine, Univ. Hosp., Univ. Lund, Lund, Sweden) Emanuelsson, H.; Mitelman, F.; Stenstam, M.; Soderstrom, N. *Acta Med Scand* 201(5): 487-489; 1977.

The case history of a 60-yr-old man who developed acute leukemia 35 yr after thorotrast angiography is presented. He had developed sarcoidosis 21 yr after the injection and myelofibrosis 34 yr after the injection. The various disorders could be attributed to the biological effects of ionizing radiation. (10 refs.)

77-4481 **Aspects of the Dosimetry of Alpha-emitting Radionuclides in Bone with Particular Emphasis on ^{226}Ra and ^{239}Pu.** (Eng.) Thorne, M. C. (Medical Res. Council Radiobiology Unit, Harwell, Didcot, Oxon. OX11 ORD, England) *Phys Med Biol* 22(1): 36-46; 1977.

Results are given for av dose rates to tissues close to endosteal surfaces and to hematopoietic bone marrow from thin plane sources of alpha-emitting radionuclides buried to different depths in bone. They demonstrate that on an activity basis, ^{239}Pu is not likely to be more than 15 times as toxic as ^{226}Ra with respect to osteosarcoma and leukemia induction. (22 refs.)

77-4482 **Strontium-90 in the Western Gulf of Mexico.** (Eng.) Payton, P. H. (Marine Biomedical Inst., Univ. Texas Medical Branch, Galveston, TX 77550) Hild, S. B.; Oertti, C. U.; Suttle, A. D. *Health Phys* 33(2): 143-145; 1977.

Measurements of ^{90}Sr in Gulf waters agree with literature values: concentrations were lower in mollusks and crabs and higher in coral than they were in water samples. The activity incorporated into shells decreased from the Galveston area southward. (11 refs.)

77-4483 **A Mathematical Model of the Accumulation of Radionuclides by Oysters (*C. virginica*) Aquacultured in the Effluent of a Nuclear Power Reactor to Include Major Biological Parameters.** (Eng.) Hess, C. T. (Dept. Physics, Univ. Maine, Orono, ME 04473) Smith, C. W.; Price, A. H. *Health Phys* 33(2): 121-130; 1977.

A mathematical model for predicting the time dependence of the specific activity of radionuclides in oysters cultured in the effluent of a nuclear power reactor has been developed to include the physical and biological half-lives of the various radionuclides, the water temperature (oyster hibernation), and shell growth. (14 refs.)

77-4484 **Inhalation of Talc Baby Powder by Hamsters.** (Eng.) Wehner, A. P. (Biology Dept., Battelle, Pacific Northwest Labs., Richland, WA 99352) Zwicker, G. M.; Cannon, W. C.; Watson, C. R.; Carlton, W. W. *Food Cosmet Toxicol* 15(2): 121-129; 1977.

Male and female Syrian golden hamsters were exposed to talc aerosol for 3, 30, or 150 min/day, 5 days/wk x 30 days, or for 30 or 150 min/day until death, or for a max of 300 days. Talc particles were deposited in the lungs; however, exposure to talc had no effect on body wt, survival, or the type, incidence, or degree of histopathological change. (31 refs.)

77-4485 **Cellular Immune Reactions after Implantation of Cellophane and in Tumorigenesis in Insects.** (Fre.) Matz, G. (Laboratoire de Biologie animale, Faculte des Sciences d'Angers, boulevard Lavoisier, F 49045 Angers Cedex, France) *Ann Parasitol Hum Comp* 52(1): 68-69; 1977.

Cellular immune reactions in insects to implantation of an inert foreign body are presented, and comparisons are made with cellular encapsulating reactions. A fragment of inert cellophane was placed in the abdominal hemolymphatic cavity of several species of insects. After 2 hr, a layer of primarily granular hemocytes surrounded the foreign body; there was no evidence of mitosis. These cells extended microtubules and microfilaments to the surface of the implant. This type of encapsulation is typical of those observed on epithelial tumors (absence of cellular proliferation and metastases, and nonfilterability). Hemocytic cellular immunity was reinforced in *Blabera craniifer* by placing the tegmental or tracheal hypoderm in the center of the hemocytic capsule; the occurrence of this phenomenon in other insects is discussed. Section of the recurrent nerve causes tumor formation by cellular multiplication of the epithelium of the affected orga at twice the normal rate and always at the level of the endo dermic structures. (6 refs.)

77-4486 **Repair Synthesis in Human Lymphocytes Pro voked by Photolysis of Ethidium Azide.** (Eng. Cantrell, C. E. (Lab. Molecular Biology, Univ. Alabama i Birmingham, Univ. Station, Birmingham, AL 35294) Yield ing, K. L. *Photochem Photobiol* 25(2): 189-191; 1977.

When human lymphocytes were mixed with 5 μM ethidium azide for 5 min in the dark and subsequently exposed to visi ble light, repair synthesis occurred, as shown by uptake o ^{3}H-thymidine in the presence of hydroxyurea. Unexposed cells showed no uptake. (9 refs.)

77-4487 **A Study of the Photoinduced Mutagenicity o Methylene Blue.** (Eng.) Gutter, B. (Dept. Mi crobiology, New York Medical Coll., Valhalla, NY 10595 Speck, W. T.; Rosenkranz, H. S. *Mutat Res* 44(2): 177-181 1977.

Salmonella typhimurium strains undergo base-substitutio mutations when illuminated in the presence of methylene blue. These mutations could be separated from those resulting from the mutagenicity of visible light. Frameshift mutations were not observed. (21 refs.)

77-4488 **The Photodynamic Immobilization of *Artemia salina* Nauplii by Polycyclic Aromatic Hydrocarbons and Its Relationship to Carcinogenic Activity.** (Eng.) Morgan, D. D. (Medical Res. 151, Veterans Admin. Hosp., 3200 Vine St., Cincinnati, OH 45220) Warshawsky, D. *Photochem Photobiol* 25(1): 39-46; 1977.

When 19 carcinogenic and 22 noncarcinogenic polycyclic aromatic hydrocarbons (PAH) were used as sensitizers for 2 and 22 hr prior to irradiation of the crustacean *Artemia salina* nauplii, the correlation of relative photodynamic activity with carcinogenic activity was excellent. Carcinogenesis by PAH may therefore result from sublethal photodynamic effects. (22 refs.)

See also:

* (Rev.): 77-4204, 77-4206, 77-4207, 77-4215, 77-4228, 77-4229, 77-4230, 77-4231, 77-4241, 77-4246, 77-4261.
* (Chem.): 77-4264, 77-4265, 77-4302, 77-4309, 77-4312, 77-4320, 77-4324, 77-4325, 77-4326, 77-4327, 77-4330, 77-4378, 77-4410, 77-4439.
* (Immun.): 77-4552, 77-4553, 77-4614.
* (Path.): 77-4630, 77-4647.
* (Epid.-Biom.): 77-4705.

77-4489 **Rous Sarcoma Virus Genome Is Terminally Redundant: The 3′ Sequence.** (Eng.) Schwartz, D. E. (Huntington Lab. Harvard Univ., Massachusetts General Hosp., Boston MA 02114) Zamecnik, P. C.; Weith, H. L. *Proc Natl Acad Sci USA* 74(3): 994-998; 1977.

A sequence of 20 nucleotide residues was determined for the region immediately adjacent to the 3′-terminal poly(A) of Rous sarcoma virus (RSV:Prague strain, subgroup C) 35S RNA by selective copying of RSV 35S RNA by reverse transcriptase from avian myeloblastosis virus. Three different short DNA oligonucleotides were obtained when synthesis was conducted in the absence of dCTP and when transcription was initiated with the site-specific primer, $dT(pdT)_8prG$. Sequence analysis of these DNA fragments gave the same nucleotide sequence for the 3′ terminus of RSV RNA as had been previously determined for the 5′ terminus. The RNA genome of this virus is, therefore, terminally redundant. (15 refs.)

77-4490 **Rous Sarcoma Virus Genome Is Terminally Redundant: The 5′ Sequence.** (Eng.) Haseltine, W. A. (Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA 02115) Maxam, A. M.; Gilbert, W. *Proc Natl Acad Sci USA* 74(3): 989-993; 1977.

The first major DNA (strong-stop DNA) made when Rous sarcoma virus (RSV: Prague strain, subgroup C) RNA is transcribed into DNA by reverse transcriptase was sequenced. This DNA is a run-off product extending 101 bases from the primer to the 5′ end of the template. The DNA sequence, therefore, determines the first 101 bases at the 5′ end of the viral RNA. In addition, because 16 contiguous bases in the transfer RNA primer are protected by the viral RNA against RNase digestion, the RNA sequence can be inferred to base 118. Twenty-one bases at the extreme 5′ end are also at the 3′ end of the virus genome and, thus, this virus is terminally redundant. On the basis of this sequence repetition at the terminal ends, mechanisms are suggested by which the growing DNA copy can jump from the 5′ end to a 3′ end of the template and become circular. The sequence also shows a possible ribosome binding site and enough secondary structure to permit a possible 5′-5′ linkage of viral RNA molecules. (37 refs.)

77-4491 **Cleavage of Rous Sarcoma Viral Polypeptide Precursor into Internal Structural Proteins In Vitro Involves Viral Protein p15.** (Eng.) von der Helm, K. (Swiss Inst. Experimental Cancer Res., Ch. des Boveresses, CH-1066 Epalinges, Lausanne, Switzerland) *Proc Natl Acad Sci USA* 74(3): 911-915; 1977.

The cleavage of Rous sarcoma virus (RSV: Prague strain, subgroup C) into internal structural proteins in vitro was studied. The 30S-40S RSV RNA was translated in a cell-free system from ascites Krebs II cells. In the absence of viral proteins p12-p27, the predominant product was the precursor polypeptide pr76, detected by autoradiography of a sodium dodecyl sulfate-polyacrylamide gel. Addition of purified p27 or p19 to the system caused no change in the translation pattern in vitro. The addition of p12 inhibited the synthesis of p76. The addition of p15, however, altered the pattern of the product formed. The pr76 band was less intense and bands representing pr66, pr53, pr34, pr32, pr29, p27, and p12 appeared, indicating the cleavage of pr76. The cleavage pattern in vitro resembled that observed in vivo by pulse-chase experiments of infected cells. Disrupted RSV also cleaved pr76 in vitro in a pattern similar to that seen with purified p15. Disrupted Rauscher murine leukemia virus did not stimulate cleavage in vitro. Autocatalytic cleavage of pr76, which contains the peptide sequence p15, was not observed. Whether the p15 protein itself is the specific processing protease or whether it activates a cellular enzyme present in the ascites cell extract was not determined. (25 refs.)

77-4492 **The Genetic Map of Rous Sarcoma Virus and Comparison of the DNA Polymerases of Avian and Murine RNA Tumor Viruses (Meeting Abstract).** (Eng.) Wang, L. A. (Univ. California, Berkeley, CA 94720) *Diss Abstr Int [B]* 38(2): 669-670; 1977. (no refs.)

77-4493 **DNA Polymerase from Intracisternal A-Type Particles of the Mouse Plasmacytoma MPC 11.** (Eng.) Schmidt, J. (Basel Institut fur Immunologie, Grenzacherstrasse 487, CH-4058 Basel, Switzerland) Pragnell, I. B.; Weimann, B. J. *Eur J Biochem* 73(2): 493-497; 1977.

Three DNA polymerases were found in intracisternal A-type particle preparations from the murine plasmacytoma MPC11. Two appeared to be related serologically to the reverse transcriptases of Rauscher leukemia virus. (22 refs.)

77-4494 **Studies of the Changes in Growth Fraction, Nuclear DNA-Polymerase, and Primer-Template**

Levels in Rauscher Leukemia (Meeting Abstract). (Eng.) Okunewick, J. P. (Allegheny General Hosp., Pittsburgh, PA 15212) *Proc Am Assoc Cancer Res* 18: 5; 1977. (no refs.)

77-4495 **Direct Measurement of the Synthesis of Viral RNA in Cells Producing C-type Viruses (Meeting Abstract).** (Eng.) Kaminchek, Y. (Weizmann Inst. Science, Rehovot, Israel) Aviv, H. *Isr J Med Sci* 13(9): 932-933; 1977. (1 ref.)

77-4496 **Role of Endogenous Murine Leukemia Virus in Immunologically Triggered Lymphoreticular Tumors. I. Development and Use of Oncogenic Cellfree Preparations Serially Passaged In Vivo.** (Eng.) Armstrong, M. Y. (Dept. Epidemiology and Public Health, Yale Univ. Sch. Medicine, 60 College St., New Haven, CT 06510) Ruddle, N. K.; Lipman, M. B.; Pierce, S. K.; Richards, F. F. *J Natl Cancer Inst* 58(1): 67-72; 1977.

Cell-free extracts (CFE's) prepared from (BALB/cJ x A/J)F_1 (CAF_1) and (BALB/cJ x C57BL/6J)F_1 ($CB6F_1$) mice with a graft-vs-host reaction (GVHR) are oncogenic but only after a mean latent period of 18 mo. Serial passage of such CFE's in successive generations of syngeneic mice inoculated at birth led to the development of two separate oncogenic preparations, the CA series in CAF_1 mice and the CB series in $CB6F_1$ mice, with a mean latent period of 6 and 12 mo, respectively. Both oncogenic preparations contained infectious B-tropic murine leukemia virus (MuLV) and particles with the ultrastructural characteristics of MuLV. When these preparations were injected into infant syngeneic mice, B-tropic MuLV could be detected in reticular tissues as early as 2 wk after inoculation. The virus persisted in the tissues and was present in the lymphoreticular tumors that subsequently developed. In young adult recipients of the virus preparations, transient MuLV replication may have occurred, but the virus subsequently disappeared from the reticular tissues and no lymphoreticular tumors developed. Previous experiments showed that MuLV was present in CFE's prepared from CAF_1 animals with the GVHR, but absent in those of normal controls. Since the lymphoreticular tumors arising in mice with the GVHR were the same as those induced by the CA and CB MuLV preparations, it was concluded that tumorigenesis in mice with the GVHR was caused by endogenous B-tropic MuLV activated by the immunologic disturbance. (22 refs.)

77-4497 **Accumulation of Viral RNA in Murine Leukemia Virus Chronically Infected Interferon-treated Cells (Meeting Abstract).** (Eng.) Bukhanashvili, M. (Bar-Ilan Univ., Ramat Gan, Israel) Aboud, M.; Salzberg, S. *Isr J Med Sci* 13(9): 932; 1977. (no refs.)

77-4498 **Inhibition of Viral RNA Synthesis in Interferon-treated Cells Infected with Murine Leukemia Virus (Meeting Abstract).** (Eng.) Aboud, M. (Bar-Ilan Univ., Ramat Gan, Israel) Salzberg, S. *Isr J Med Sci* 13(9): 931; 1977. (no refs.)

77-4499 **Arrangement of Viral Sequences in Chromatin (Meeting Abstract).** (Eng.) Cedar, H. (Hebrew Univ. Jerusalem, Jerusalem, Israel) Panet, A. *Isr J Med Sc* 13(9): 938; 1977. (no refs.)

77-4500 **Binding of Transfer RNA to RNA Tumor Virus Reverse Transcriptase (Meeting Abstract).** (Eng.) Panet, A. (Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel) Weil, G.; Berliner, H.; Tal, B.; Friis, R. R. *Isr J Med Sci* 13(9): 932; 1977. (no refs.)

77-4501 **The Diversity and Specificity of Nuclear an Polysomal Poly(A)+ RNA Populations in Normal and MSV-transformed Cells.** (Eng.) Rolton, H. A. (Beatson Inst. Cancer Res., Wolfson Lab. Molecular Pathology Garscube Estate, Switchback Road, Bearsden, Glasgow, G61 1BD, Scotland) Birnie, G. D.; Paul, J. *Cell Differ* 6(1): 25-39 1977.

Molecular hybridization kinetics were studied to determine qualitative and/or quantitative changes in nuclear and polysomal poly(A)+ RNA sequences caused by an oncogenic virus. Nuclear and polysomal poly(A)+ RNA's were isolated from untransformed BALB/c 3T3 cells and murine sarcoma virus-transformed, non-virus producer BALB/c 3T3 cells (MSV/3T3), and the complementary DNA's were transcribed from them. Homologous and heterologous hybridization reactions for nuclear poly(A)+ indicated that the relative abundance of most of the RNA sequences was the same in both cell types. Particularly surprising, in view of the marked differences in 3T3 and MSV/3T3 cell morphology and growth characteristics, was the finding that at least 95% of polysomal poly(A)+ RNA consisted of sequences common to both 3T3 and MSV/3T3 cells. 3T3 cell transformation was accompanied by an increase in the abundance of a population of RNA sequences that were present in small quantities on polysomes of untransformed cells, together with a concomitant decrease in the abundance of other RNA se-

ences. Posttranscriptional control appears to have been al-
ed either by or following transformation. (28 refs.)

-4502 **Enhancement of Tumor Induction in Rats with Moloney Murine Sarcoma Virus by a 'New'
ethod Based on Direct Injection into Fetuses.** (Eng.) Hira-
, T. (1-14-2, Minami-Tanaka, Nerima-ku, Tokyo 177, Ja-
n) Miyajima, H.; Watanabe, T.; Tsukuda, R.; Shimamoto,
. *J Natl Cancer Inst* 58(1): 73-82; 1977.

n day 18 of gestation, Sprague-Dawley rat fetuses were in-
cted with 0.025 ml of Moloney murine sarcoma virus (M-
SV) diluted one-, five-, or twenty-fivefold; the virus was
jected directly into the dorsal sc region through the uterine
all. Within 8 wk after birth, 52 (86.7%) of 60 animals sur-
ving the highest M-MSV dose developed tumors, as did 13
2.5%) of 40 animals surviving the fivefold dilution. No tu-
ors were induced with the lowest dose. When a one-fifth
ilution of the virus preparation was inoculated at fetal ages
6, 18, and 20 days, the incidence of lesions decreased with
dvancing fetal age. The tumors developed preferentially at
e virus inoculation site and/or in the proximal parts of the
xtremities; all were of mesenchymal derivation, ie, malig-
ant mesenchymoma, rhabdomyosarcoma, osteosarcoma, fi-
rosarcoma or fibromyxosarcoma, hemangiosarcoma, plas-
acytoma, and a giant cell tumor. (16 refs.)

7-4503 **Glucocorticoid-stimulated Accumulation of Mouse Mammary Tumor Virus RNA: Increased
ate of Synthesis of Viral RNA.** (Eng.) Ringold, G. M.
Dept. Biochemistry, Univ. California, San Francisco, CA
4143) Yamamoto, K. R.; Bishop, J. M.; Varmus, H. E. *Proc
Vatl Acad Sci USA* 74(7): 2879-2883; 1977.

The effect of glucocorticoid hormones on the rate of synthesis
of mouse mammary tumor virus (MMTV) RNA was investi-
gated in a cultured cell line from a GR mouse mammary
carcinoma (GR), in an MMTV-infected rat hepatoma cell
ine (HTC), and in S49 lymphoma cells derived from a
BALB/c mouse lymphoma. The effect of dexamethasone, a
synthetic glucocorticoid, on the rate of MMTV RNA synthe-
is was measured directly using a molecular hybridization
echnique that vastly reduces hybridization backgrounds,
permitting specific detection of low levels of labeled RNA.
n GR cells, the hormone caused a tenfold increase in the
synthesis rate of MMTV RNA without appreciably affecting
he overall rate of cellular RNA synthesis. Transition from
he basal to the maximally stimulated rate of MMTV RNA
synthesis occurred within 0-15 min after hormone addition.
Similar results were seen with the HTC. It appears, therefore,
hat glucocorticoids regulate MMTV genes principally by
his rapid and specific alteration of their transcription rate.
Dexamethasone did not affect the rate of viral RNA synthesis in the S49 lymphoma cells. These results provide direct evidence that small molecules, in this case steroid hormones, may affect the rate of specific transcription in eukaryotic cells, as has already been shown for prokaryotic systems. (31 refs.)

77-4504 **Organ Distribution of Exogenous Murine Mammary Tumour Virus as Determined by Bioassay.** (Eng.) Bentvelzen, P. (Radiobiological Inst. TNO, Lange Kleiweg 151, Rijswijk, The Netherlands) Brinkhof, J. *Eur J Cancer* 13(3): 241-245; 1977.

Cell-free mammary tumor virus activity was exhibited by extracts from the following organs of exogenously infected BALB/cfC3H mice: salivary gland, kidney, testis, and epididymis. This was shown by bioassay in female BALB/c mice, which were then forced bred for mammary tumor production. Mammary tumor-inducing activity was demonstrated for intact cells of thymus, spleen, bone marrow, and liver. Radiation (3,000 rads) largely destroyed the cell-bound viral activity. No cell-free or cell-bound activity was found in lung, brain, or pancreas. The results illustrate the importance of epigenetic factors in the expression of exogenous mammary tumor virus. (27 refs.)

77-4505 **A Quantitative Analysis of the Rescue Procedure of RNA Sequence by Mammalian Type C Viruses (Meeting Abstract).** (Eng.) Levin, R. (Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel) Goldberg, R. J. *Isr J Med Sci* 13(9): 932; 1977. (no refs.)

77-4506 **Analysis of Feline RNA Tumor-virus Specific Gene Expression in Various Types of Cat Neoplasia (Meeting Abstract).** (Eng.) Levin, R. (Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel) Scolnick, E. M. *Isr J Med Sci* 13(9): 931; 1977. (no refs.)

77-4507 **Excretion of Feline Leukaemia Virus by Naturally Infected Pet Cats.** (Eng.) Francis, D. P. (Dept. Microbiology, Harvard Sch. Public Health, Boston, MA) Essex, M.; Hardy, W. D. *Nature* 269(5625): 252-254; 1977.

A study of feline leukemia virus (FeLV) infected healthy cats was performed to determine the method of virus transmission. The cats excreted FeLV in their saliva in titres that were as high as or higher than those in the blood plasma. Other body fluids are probably less significant in virus transmission. It is suggested that epidemiological investigations of the link between FeLV and human disease include nonleukemic pet cats, which may be potentially infectious. (20 refs.)

77-4508 **Virus Isolation Test for Feline Leukemia Virus.** (Eng.) de Noronha, F. (Oncology Lab., Pathology Dept., New York State Coll. Veterinary Medicine, Cornell Univ., Ithaca, NY 14853) Poco, A.; Post, J. E.; Rickard, C. G. *J Natl Cancer Inst* 58(1): 126-131; 1977.

Feline leukemia virus (FeLV) infection in cats can be detected by coculturing separated blood lymphocytes and platelets with clone 81 cells, which carry a murine sarcoma genome but are free of leukemia virus (S+L-). FeLV caused cell transformation that was easily visible 3-12 days after infection. This method is simple, sensitive, and easily read: it has the advantage of directly detecting infectious FeLV rather than viral antigens. (18 refs.)

77-4509 **Feline Oncornavirus-associated Cell-Membrane Antigen (FOCMA): Distinction Between FOCMA and the Major Virion Glycoprotein.** (Eng.) Stephenson, J. R. (Lab. RNA Tumor Viruses, NCI, Bethesda, MD 20014) Essex, M.; Hino, S.; Hardy, W. D.; Aaronson, S. A. *Proc Natl Acad Sci USA* 74(3): 1219-1223; 1977.

Sera from cats exposed to feline leukemia virus (FeLV) were analyzed with respect to their serologic reactivities against both feline oncornavirus-associated cell-membrane antigen (FOCMA) and the FeLV structural proteins gp70 and p30. Using membrane immunofluorescence and radioimmunoprecipitation assays, the antibody response to FOCMA was found to be independent of the antibody response to gp70 and p30. Antibody to gp70 and p30 was never found in serum samples from viremic cats, even though such cats frequently exhibited high FOCMA antibody titers. In studies with sequential serum samples from an FeLV-exposed cat, FOCMA antibody was first detected 15 wk prior to the development of significant antibody titers to either gp70 or p30. Viremic cats with high FOCMA antibody titers demonstrated levels of circulating viral antigens similar to those in viremic cats that lacked detectable FOCMA antibody. This lack of correlation between amounts of virus antigens and FOCMA antibody titer suggests that gp70 and p30 do not absorb FOCMA antibody in vivo. Exhaustive absorption of antiserum that had antibody to FOCMA, gp70, and p30 with purified gp70 or p30 markedly reduced antibody activity to these virion structural proteins without reduction in FOCMA antibody activity. These results indicate that FOCMA is not one of these major FeLV structural proteins. (40 refs.)

77-4510 **Replication Process of the Parvovirus H-1.**
Characterization of a Replication Terminus
H-1 Replicative-form DNA. (Eng.) Rhode, S. L. (Putna
Memorial Hosp. Inst. for Medical Res., Bennington,
05201) *J Virol* 21(2): 694-712; 1977.

Escherichia coli restriction endonuclease EcoRI was used
characterize the replicative form DNA of the parvovirus H
The findings indicate that the structure of the replication t
minus at the left end of the molecule is similar to that recen
proposed for the adenovirus-associated virus DNA termi
(28 refs.)

77-4511 **Replication Process of the Parvovirus H-1. V**
Electron Microscopy of Replicative-form D
Synthesis. (Eng.) Singer, I. I. (Putman Memorial Hosp. In
for Medical Res., Bennington, VT 05201) Rhode, S. L. *J Vi*
21(2): 713-723; 1977.

Electron microscopic observations of the replicative form
parvovirus H-1 DNA revealed that it is Y-shaped, with
origin of replication no more than 0.15 genome lengths fr
one end. The end near the origin of replication did not app
to be complementary to the other end as in the case
adenovirus associated virus. (24 refs.)

77-4512 **Replication Process of the Parvovirus H**
VIII. Partial Denaturation Mapping and Loc
ization of the Replication Origin of H-1 Replicative-fo
DNA with Electron Microscopy. (Eng.) Singer, I. I. (Putna
Memorial Hosp. Inst. for Medical Res., Bennington,
05201) Rhode, S. L. *J Virol* 21(2): 724-731; 1977.

Mapping and electron microscopic studies of parvovirus H
DNA replication indicated that the origin of replication
approx 300 base pairs from the right end of the molecu
which had a relatively high guanine plus cytosine conte
The other end of the molecule had a high adenine plus th
mine content. (13 refs.)

77-4513 **New Oncogenic Papova Virus from Prim**
Cells. (Eng.) Waldeck, W. (Institut fur Virusf
schung, Deutsches Krebsforschungszentrum, 6900 Heid
berg, W. Germany) Sauer, G. *Nature* 269(5624): 171-1
1977.

A new papova virus, capable of rapidly transforming cells
vitro, has been isolated from VERO-cells (a permanent l

derived from monkey kidney cells). The virus, designated HD-virus, did not display any recognizable cytopathogenic effect on the VERO-cells harboring it. (13 refs.)

77-4514 **Modification of Hydroxyindole-O-methyltransferase Activity in Experimental Pineocytomas Induced in Hamsters by a Human Papovavirus (JC).** (Eng.) Quay, W. B. (Waisman Center on Mental Retardation and Human Development, Univ. Wisconsin, Madison, WI 53706) Ma, Y. H.; Varakis, J. N.; ZuRhein, G. M.; Padgett, B. L.; Walker, D. L. *J Natl Cancer Inst* 58(1): 123-127; 1977.

Hydroxyindole-O-methyltransferase (HIOMT) activity was studied and compared in seven pineal tumors (pineocytomas) induced in vivo in Syrian hamsters after postnatal inoculation (0.02 ml, intracerebrally) with the MAD-4 strain of human JC papovavirus. Levels of tumor HIOMT activity were correlated with the degree of cytologic differentiation of the pineocytes of each neoplasm, as judged from electron micrographs. The relative capacities of the HIOMT in the tumors to methylate three related substrates (N-acetylserotonin, 5-hydroxytryptophol, and 5-hydroxytryptamine) gave similar ratios in the individual tumors and were not different from those of HIOMT in normal hamster pineal glands. (18 refs.)

77-4515 **Characterization of Polyoma Virus T Antigen.** (Eng.) Ito, Y. (Dept. Cell Regulation, Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England) Spurr, N.; Dulbecco, R. *Proc Natl Acad Sci USA* 74(3): 1259-1263; 1977.

High-titer antiserum raised in rats against the tumor (T) antigen of polyoma virus was used to purify the T antigen by the Staphylococcus protein A antibody absorbent (PAA) technique. The major component of this antigen was identified both in lytic infection and in transformed rat cells as a protein with an apparent molecular wt of 100,000-108,000 in sodium dodecyl sulfate/polyacrylamide gel electrophoresis. In cells infected by temperature-sensitive (ts) A mutants, this component was ts. Several minor components were also observed. They were of two types: A-mutation sensitive components, which decayed as did the major component at high temperature in cells infected by ts A mutants, and A-mutation insensitive components, which did not appreciably decay under the same conditions. In pulse and chase experiments there was a slight decrease in electrophoretic mobility of T antigen during the chase period at the permissive temperature. In polyoma-transformed cells, the amounts of T antigen appeared to be far less than in lytically infected cells, both by immunofluorescence and the PAA technique, but the size of the antigen appeared to be the same. The much-reduced amount of T antigen in transformed cells suggests that its primary role is for lytic infection, probably viral DNA replication. The role it plays in transformation is more obscure. (26 refs.)

77-4516 **Giant RNA Molecules in Polyoma Infected Cells: Mapping of Virus-specific Sequences Relative to the Poly(A) Segment (Meeting Abstract).** (Eng.) Lev, Z. (Technion-Israel Inst. Technology, Haifa, Israel) Manor, H.; Kamen, R. *Isr J Med Sci* 13(9): 933; 1977. (no refs.)

77-4517 **Purification and Properties of an Endonuclease from Nuclei of Cells Infected with Polyoma Virus (Meeting Abstract).** (Eng.) McGuire, M. S. (Kansas State Univ., Manhattan, KS 66502) *Diss Abstr Int [B]* 38(2): 518; 1977. (no refs.)

77-4518 **In Vitro Characteristics and Oncogenicity of Some Cell Lines Derived from BK Virus-transformed Hamster Kidney Cells (Meeting Abstract).** (Ita.) Possati, L. (Istituto di Microbiologia, Universita di Ancona, Ancona, Italy) Honorati, M. C.; Portolani, M. *Ann Sclavo* 18(6): 881-882; 1976. (no refs.)

77-4519 **Characteristics of Hamster, Mouse and Monkey Cells Transformed by BK Virus (New Human Papova Virus) (Meeting Abstract).** (Ita.) Cassai, E. (Istituto di Microbiologia, Universita di Ferrara, Ferrara, Italy) Barbanti Brodano, G.; Portolani, M.; Borgatti, M.; Corallini, A.; Grossi, M. P.; Tampieri, M. *Ann Sclavo* 18(6): 877; 1976. (no refs.)

77-4520 **"Minichromosomes" of Animal Viruses: Studies of DNA-Nuclear Protein Complexes (Meeting Abstract).** (Eng.) Pignatti, P. F. (Istituto di Genetica e Laboratorio di Genetica Biochimica ed Evoluzionistic del Consiglio Nazionale delle Ricerche, Pavia, Italy) Meneguzzi, G.; Milanesi, G. *Ital J Biochem* 26(1): 71; 1977. (no refs.)

77-4521 **Tumorigenicity of Simian Virus 40-transformed Human Cells and Mouse-Human Hybrids in Nude Mice.** (Eng.) Koprowski, H. (Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA 19104) Croce, C. M. *Proc Natl Acad Sci USA* 74(3): 1142-1146; 1977.

The tumorigenic properties of four different human cell lines transformed by simian virus 40 (SV40) were compared with those of hybrids resulting from the fusion of these SV40-transformed human cells and normal mouse peritoneal macrophages (MPM) to determine if the hybrid cells are more tumorigenic for athymic nude mice than the transformed human parental cells. Two of the transformed human cell lines, W18Va2 and GM52VA, were tumorigenic when injected at a concentration of 1 x 10^7 cells per mouse. The other two cell lines, LN-SV and GM54VA, induced very small tumors only after the injection of 1 x 10^8 cells per mouse. Cells recovered from tumors were grown in tissue culture and studied for expression of SV40 tumor (T) antigen and expression of five human isozymes (nucleoside phosphorylase, mannosephosphate isomerase, superoxide dismutase-1, glutamic oxaloacetic transaminase, and β-glucuronidase). All cell lines that were recovered from the tumors were human, and they expressed the human forms of the isozymes. They were also all positive for SV40 T antigen. Somatic cell hybrids between either LN-SV or GM54VA SV40-transformed human cells and C57BL and BALB/c MPM, which have retained the human chromosomes carrying the SV40 genome, were much more tumorigenic in nude mice (LN-SV x C57BL: 5/20; LN-SV x BALB/c MPM: 20/20; GM54VA x C57BL: 13/13; GM54VA x BALB/c MPM: 9/9) than in the SV40-transformed human cell parents. These experiments suggest that the genetic background in which the human chromosomes carrying the SV40 genome are present plays a role in modulating the expression of malignancy. (19 refs.)

77-4522 **Interferon Inhibits the In Vitro Accumulation of Virus Specific RNA in Nuclei Isolated from SV40 Infected Cells.** (Eng.) Metz, D. H. (Natl. Inst. Medical Res., Mill Hill, London NW7 1AA, England) Oxman, M. N.; Levin, M. J. *Biochem Biophys Res Commun* 75(1): 172-178; 1977.

The mechanism by which interferon (IF) inhibits simian virus 40 (SV40) replication was investigated using an in vitro system consisting of nuclei from infected Vero cells that in the presence of cytosine arabinoside synthesize early SV40 RNA. The in vitro synthesis of SV40-specific RNA was almost completely blocked by low doses of α-amanitin, but total RNA synthesis was only partially inhibited. The accumulation of viral RNA was blocked in nuclei prepared from cells pretreated with IF prior to infection and incubated in a reaction mixture containing 100 milliM KCl. This resembled the situation in intact cells. When the reaction mixture contained 300 milliM KCl, however, the IF-induced block in viral RNA accumulation was reversed. Two possible explanations are offered for the effect of IF treatment on the accumulation of early viral transcripts in SV40-infected cells. First, IF treatment may induce the formation of an intracellular inhibitor that blocks viral transcription; elevated salt concentratio
in vitro might then displace the inhibitor and permit tra
scription of the viral genome. Second, the reduced accumul
tion of early viral RNA may be due to enhanced degradatio
within the nucleus of the IF-treated cell effected by a ribon
clease specific for viral, but not for most cellular RNA. Th
putative nuclease might be inactivated at elevated ion
strength, resulting in the increased level of SV40-specif
RNA seen in nuclei incubated with 300 milliM KCl in vitr
These two possibilities cannot be distinguished at present. (1
refs.)

77-4523 **Structure of a Large Segment of the Genome o
Simian Virus 40 That Does Not Encode Know
Proteins.** (Eng.) Dhar, R. (Lab. Biology Viruses, NCI, NIH
Bethesda, MD 20014) Subramanian, K. N.; Pan, J.; Weiss
man, S. M. *Proc Natl Acad Sci USA* 74(3): 827-831; 1977.

The nucleotide sequence of the DNA region of simian viru
40 (SV40) extending from 0.595 to 0.790 map unit has bee
derived. The analysis was performed primarily by transcrip
tion of restriction endonuclease DNA fragments, followed b
RNA sequence analysis and by limited exonuclease digestio
of terminally labeled DNA fragments. The sequenc
analyzed includes the DNA complementary to the 5′ end o
early messenger RNA (mRNA) and to the 5′ end of som
of the forms of late RNA. The distribution of terminatio
codons in transcripts of the viral genome is such that a con
tiguous stretch of 17% (almost 800 nucleotides) of the vira
DNA could not code for known viral proteins. Transcriptio
of the DNA sequence produces an RNA that, if translate
would direct the synthesis of peptides shorter than any of th
known viral proteins. RNA complementary to this DNA re
gion was found in the cytoplasm of infected cells. Analysi
of the sequence of late strand RNA suggests that this RN
is not covalently linked to the mRNA that encodes structura
proteins. The nucleotide sequence of this region of SV4
DNA contains several examples of repeated sequences tha
may be analogous to reiterated sequences in host cell DNA
(22 refs.)

77-4524 **Nucleotide Sequence of the SV40 DNA Restric
tion Fragment Hind C-Hap 2.** (Eng.) Van Heu
verswyn, H. (Lab. Molecular Biology, Univ. Ghent, Lede
ganckstraat, 39, 9000 Ghent, Belgium) Van de Voorde, A.
Fiers, W. *Nucleic Acids Res* 4(4): 1015-1024; 1977.

The simian virus 40 DNA fragment Hind C-Hap 2 was la
beled at the 5′-ends by polynucleotide kinase and γ-^{32}P-AT
and digested with a suitable restriction enzyme. The separat
products were then partially degraded with the base-specifi
reagents dimethyl sulfate or hydrazine and then analyzed o
polyacrylamide gel. The Hind C-Hap 2 sequence is 126 bas

airs long, and one of the three possible reading frames for anslation does not contain any termination codon. Thus, though no protein is known to be encoded by this region, e possibility cannot be ruled out completely. The sequence so contains several AT-rich blocks. (16 refs.)

7-4525 **Study of Alkaline Phosphatase Activity of Normal Hamster Fibroblasts and Those Trans- rmed by SV40 Virus. Effect of Cyclic AMP.** (Fre.) Ma- ere, J. C. (CHU Saint-Antoine, Service de Chimie iologique, 27, rue Chaligny - 75571 Paris Cedex 17) Ma- ere, C.; Polonovski, J. *Biochimie* 59(2): 221-223; 1977.

he alkaline phosphatase activity of normal (EHB) and simi- n virus 40 (SV40)-transformed hamster fibroblasts (EHSVi) as measured in the presence and absence of dibutyryl cyclic MP and/or theophylline. The fibroblasts were cultured in inimal essential medium with added tryptose phosphate roth, glucose, glutamine, penicillin, streptomycin, and calf erum. Initial seeding of cultures was with 30,000 cells/cm^2 AMP was added in concentrations of 10^{-3} -10-5 M, with r without theophylline, 10^{-4} M, 1 day after seeding. Alkaline hosphatase activity of homogenates of the EHSVi fibrob- asts, measured on days 1-5, was low (10 nanomoles/hr/mg rotein) and constant. Addition of cAMP and/or theophyl- ne had little or no effect. However, these compounds arkedly increased the enzyme activity of EHB homogenates 200 nanomoles/hr/mg protein on day 4. The increase in hosphatase activity seemed to require protein synthesis, be- ause addition of 3.6 x 10^{-6} M cycloheximide diminished en- yme levels immediately. It is suggested that alkaline phos- hatase activity is related to inhibition of cell contact, which as absent in the SV40-transformed fibroblasts. (13 refs.)

77-4526 **Effects of db-cAMP and Theophylline on Concanavalin A Binding Site Distribution on Trans- formed and Protease-treated Cell Lines.** (Eng.) Borysenko, . Z. (Dept. Anatomy, Tufts Univ. Sch. Medicine, Boston, MA 02111) Ukena, T. E.; Karnovsky, M. J. *Exp Cell Res* 107(2): 253-260; 1977.

The effects of dibutyryl cyclic AMP (db-cAMP) and theophylline on the surface distribution of concanavalin A binding sites (CABS) on 3T3 cells, simian virus 40 (SV40)-transformed 3T3 cells (SV3T3), and SV40-transformed mouse embryo fibroblast (VLM) were examined. Overnight incubation of VLM cells in medium containing db-cAMP and theophylline (both at 10^{-3} M) completely eliminated the lectin-induced clustering of CABS on many transformed cell lines. Similar treatment of SV3T3 cells caused a partial inhibition of clustering. A clone of 3T3 cells that did not normally show lectin-induced clustering could be caused to patch by brief trypsinization. Induction of clustering on these cells after trypsization was also prevented by db-cAMP and theophylline. The possibility that the db-cAMP and theophylline-induced restoration of normal CABS distribution may be modulated by stabilization of a microtubular protein is discussed. (41 refs.)

77-4527 **In Vitro Inhibition of Viral DNA Polymerase Activity by Litmomycin.** (Eng.) Sethi, M. L. (Dept. Biomedicinal Chemistry, Coll. Pharmacy Pharmacal Sciences, Howard Univ., Washington, DC 20059) *J Pharm Sci* 66(1): 130-132; 1977.

The effect of litmomycin on the purified protein fraction of reverse transcriptase from RNA tumor viruses was assessed. The inhibition of DNA polymerase activity from murine leukemia virus, simian sarcoma virus type 1, and avian myeloblastosis virus at increasing concentrations of litmomycin (0-240 μg/ml) was undertaken. The enzyme activity gradually declined with increasing litmomycin concentration. The inhibition curves for all three viruses were similar. Fifty percent inhibition was obtained with 80-100 μg/ml. To explain the mode of enzyme inhibition, different template primers such as polyriboadenylate-oligodeoxythymidylate (I), polydeoxyadenylate-oligodeoxythymidylate (II), polyribocytidylate-oligodeoxyguanylate (III), activated DNA, and RNA with a sedimentation constant of 70S were used. Different degrees of enzyme inhibition were obtained with different template primers. A high degree of inhibition in the presence of I or II, as compared to III, could be due to a strong binding affinity of litmomycin with adenine-thymine template primers. Effects of increasing concentrations of avian myeloblastosis virus DNA polymerase and template primer were observed on the litmomycin-inhibited reaction mixture. The activity of the litmomycin-inhibited reaction mixture was restored linearly when I was increased from 2 to 20 μg and the enzyme concentration was increased from 5 to 20 μl. When litmomycin was added at 5 and 10 min after initiation of the polymerization reaction, the enzyme activity continued for approx 20 min, comparable to the control. However, when the litmomycin was added after 20 min, the enzyme activity stopped instantly, as indicated by ^{3}H-thymidine monophosphate incorporation. Litmomycin inhibits DNA polymerase activity of RNA tumor viruses by interaction with (riboadenylate)n-(deoxythymidylate)n or adenine-thymine bases and (ribocytidylate)n-(deoxyguanylate)n or cytosine-guanine bases to a different degree of binding. (19 refs.)

77-4528 **Cellular and Cell-free Synthesis of SV40 T Antigen (Meeting Abstract).** (Eng.) Prives, C. (Weizmann Inst. Science, Rehovot, Israel) Gluzman, Y.; Beck, Y.; Revel, M.; Winocour, E. *Isr J Med Sci* 13(9): 934-935; 1977. (no refs.)

77-4529 **Cell-free Translation of Simian Virus 40 Early Messenger RNA Coding for Viral T-Antigen.** (Eng.) Prives, C. (Dept. Virology, Weizmann Inst. Science, Rehovot, Israel) Gilboa, E.; Revel, M.; Winocour, E. *Proc Natl Acad Sci USA* 74(2): 457-461; 1977.

Simian virus 40 (SV40) messenger RNA (mRNA) was isolated by hybridization of cytoplasmic RNA extracted from SV40-infected BS-C-1 monkey cells early in lytic infection, to SV40 DNA immobilized on Sepharose. The early viral mRNA, when added to a wheat-germ translation system, directed the synthesis of a unique class of products, including a 90,000 molecular wt (MW) polypeptide. This 90,000 MW product and a prominent 17,000 MW polypeptide could be specifically immunoprecipitated with hamster antiserum to SV40 T antigen, but not with hamster control serum. Similar immunoprecipitation of extracts of SV40-infected cells with hamster anti-T serum yielded 90,000 MW and 17,000 MW polypeptides; these polypeptides were not found in immunoprecipitates of uninfected cell extracts. SV40 complementary RNA (cRNA), prepared by asymmetric transcription of plaque-purified SV40 DNA, directed the cell-free synthesis of several products, including a 70,000 MW polypeptide that could be specifically immunoprecipitated with anti-T serum. However, no T antigen-related polypeptide was found in infected cells that corresponded in size to the major immunoprecipitated cRNA product. Simian of cy early viral synthesis wt po could T ant of ex 90,000 in im RNA (DNA, a 70, with in in cRNA (39 refs.)

77-4530 **Identification of Simian Virus 40 Tumor and U Antigens.** (Eng.) Robb, J. A. (Dept. Pathology, Univ. California at San Diego, La Jolla, CA 92093) *Proc Natl Acad Sci USA* 74(2): 447-451; 1977.

The synthesis and identity of simian virus 40 (SV40) T (tumor) and U (early) antigens were examined during productive infection in monkey cells, abortive infection in mouse cells, and in SV40-transformed mouse cells. Sodium dodecyl sulfate/polyacrylamide slab gel electrophoresis of ^{35}S-methionine-labeled radioimmune precipitates demonstrated that the T and U antigenic sites were on the same 94,000, 89,000, and 84,000 molecular wt species detected during productive infection, a 94,000 species made during abortive infection, and a 94,000 species found in transformed cells. The 94,000 species was relatively unstable compared with the relatively stable 89,000 and 84,000 species produced during productive infection. The stable 89,000 and 84,000 species were differentially extracted from productively infected cells, which suggests an intracellular compartmentation and/or different affinities of these species for cellular substrates. The 94,000 species synthesized during abortive infection was more stable than the comparable 94,000 species synthesized in transformed cells. Three temperature-sensitive A group mutants produced several unstable species of T antigen at the restrictive temperature. (38 refs.)

77-4531 **Catecholamine Hormone Receptor Differences Identified on 3T3 and Simian Virus-transformed 3T3 Cells.** (Eng.) Sheppard, J. R. (Dight Inst. Human Genetics, Dept. Genetics and Cell Biology, Univ. Minnesota, Minneapolis, MN 55455) *Proc Natl Acad Sci USA* 74(3): 1091-1094; 1977.

A catecholamine (β-adrenergic) hormone receptor site was identified on 3T3 and simian virus 40 (SV40)-transformed 3T3 cells (SV3T3) using the direct binding of a radiolabeled antagonist, (-)-^{3}H-alprenolol, to crude membrane preparations and a physiological response (cellular cyclic AMP levels) to exposure to the catecholamines epinephrine, norepinephrine, and isoproterenol. At a concentration of 1 μM, epinephrine and isoproterenol elevated cellular cyclic AMP levels 8- and 12-fold, respectively, in both cell lines. Norepinephrine was also a potent agonist on 3T3 cells (8-fold stimulation), but SV3T3 cells showed a lesser (2-fold) response to this hormone. The specificity of the physiological response is indicated by the increased effectiveness of (-) compared to (+) stereoisomers, rapid and reversible kinetics (steady state within 2 min), high affinity, and saturability. These hormone receptor studies indicate that the 3T3 cells have a β adrenergic receptor but that the SV3T3 cells have a receptor with β qualities. The number of β-adrenergic hormone receptors in normal 3T3 cells appears to be two times that in SV3T3 cells per milligram of membrane protein. (31 refs.)

77-4532 **Protein Constituents of Nuclear Ribonucleoprotein from Normal and Virus-SV40-infected Cells (Meeting Abstract).** (Eng.) Pagoulatos, G. N. (Lab. Oncogenic Viruses, Dept. Molecular Biology, Pasteur Inst., Paris, France) Yaniv, M. *Biochem Soc Trans* 5(3): 671-672; 1977. (3 refs.)

77-4533 **Endogenous Type C Virus Expression in Murine Cells Transformed by Simian Virus 40 (Meeting Abstract).** (Eng.) Turner, S. (Univ. California, Berkeley, CA 94720) *Diss Abstr Int [B]* 38(2): 524; 1977. (no refs.)

77-4534 **Natural Human Antibodies Reactive with Primate Type-C Viral Antigens.** (Eng.) Kurth, R. (Friedrich-Miescher-Laboratorium, Max-Planck-Insts., Spemannstrasse 37, 74 Tubingen, W. Germany) Teich, N. M.; Weiss, R.; Oliver, R. T. *Proc Natl Acad Sci* 74(3): 1237-1241; 1977.

A survey of human sera from healthy individuals revealed ie presence of naturally occurring antibodies that reacted radioimmunoprecipitation assays with mammalian C-type ruses. Of 39 sera tested, 100% showed reactivity against aboon endogenous virus (BEV), but 49% showed reactivity gainst simian sarcoma-associated virus (SSAV). Polyacrylaide gel electrophoresis of immune precipitates revealed the resence of the viral proteins gp70, p28, and p15. There were w, but detectable, levels of antibody to the major internal rotein of murine leukemia virus, but no activity against the ructural proteins of avian sarcoma virus. The reactions apeared to be mediated by IgG, because IgG purified from everal human sera precipitated viral antigen as effectively s the corresponding volume of whole serum. These studies rovide indirect evidence that the infectious mode of transission remains a real possibility in humans, and they suggest hat infection with an oncornavirus may be widespread. (38 efs.)

7-4535 **Characterization of a Retravirus Isolated from Squirrel Monkeys.** (Eng.) Schochetman, G. (Vial Oncology Program, NCI, Frederick Cancer Res. Center, rederick, MD 21701) Fine, D.; Arthur, L.; Gilden, R.; Heerling, R. *J Virol* 23(2): 384-393; 1977.

he antigenic and biochemical properties of SMRV, a new etravirus isolated from the squirrel monkey, *Saimiri ciureus*, are compared to those of other retraviruses. he retravirus is the first isolate from New World ionkeys. It appears to be endogenous to this species. 29 refs.)

7-4536 **Establishment of an Epstein-Barr Virus (EBV)-Negative B-Cell Lymphoma Line from a Japaiese Burkitt Lymphoma (BL) and Its Serial Passage in Hamsters (Meeting Abstract).** (Eng.) Miyoshi, I. (Dept. Medicine,)kayama Univ. Medical Sch., Okayama, Japan) Matsuda, .; Kishimoto, H.; Kimura, I. *Proc Am Assoc Cancer es* 18: 12; 1977. (no refs.)

7-4537 **DNA of Epstein-Barr Virus. II. Comparison of the Molecular Weights of Restriction of Enlonuclease Fragments of the DNA of Epstein-Barr Virus itrains and Identification of End Fragments of the B95-8 itrain.** (Eng.) Hayward, S. D. (Dept. Medicine, Committee in Virology, Univ. Chicago, Chicago, IL 60637) Kieff, E. *J irol* 23(2): 421-429; 1977.

ncubation of the DNA of B95-8 strain Epstein-Barr virus EBV (B95-8) DNA] with *Eco*RI, *Hsu* I, *Sal* I, or *Kpn* I estriction endonuclease yielded 8 to 15 fragments separable in 0.4% agarose gels and ranging in molecular wt from < 1 to $> 30 \times 10^6$. *Bam* I and *Bgl* II yielded fragments $< 11 \times 10^6$. Preincubation of EBV (B95-8) DNA with lambda exonuclease resulted in a decrease in the *Hsu* I A and *Sal* I A and D fragments, indicating that these fragments are positioned near termini. The electrophoretic profiles of the fragments produced by cleavage of the DNA of the B95-8, HR-1, and Jijoye strains of EBV were each distinctive. The molecular wts of some *Eco*RI, *Hsu* I, and *Sal* I fragments from the DNA of the HR-1 strain of EBV [EBV (HR-1) DNA] and of *Eco*RI fragments of the DNA of the Jijoye strain of EBV were identical to those of fragments produced by cleavage of EBV (B95-8) DNA with the same enzyme, but others were unique to each strain. Some *Hsu* I, *Eco*RI, and *Sal* I fragments of EBV (HR-1) DNA and *Kpn* I fragments of EBV (B95-8) DNA were present in half-molar abundance relative to the majority of the fragments. In these instances, the sum of the molecular wts of the fragments was $> 10^8$, the known molecular wt of EBV (HR-1) and (B95-8) DNA. The simplest interpretation of this finding is that each EBV (HR-(HR-1), and possibly also (B95-8), DNA preparation contains two populations of DNA molecules that differ in the arrangement of DNA sequences about a single point, as has been described for herpes simplex virus DNA. Minor fragments could also be observed if there was more than one difference in primary structure of the DNA's. The data do not exclude more extensive heterogeneity in primary structure of the DNA of the HR-1 strain. However, the observation that the relative molar abundance of major and minor fragments of EBV (HR-1) DNA did not vary between preparations from cultures that had been maintained separately for several years favors the former hypothesis over the latter. (31 refs.)

77-4538 **Experimental Transmission of VT4 Oncogenic Virus by Larvae of *Aedes aegypti* Raised in a Culture Medium.** (Fre.) Tran Ba Loc, P. (Laboratoire de Zoologie et de Cancerologie Experimentale, Faculte de Medecine et de Pharmacie 4, Place Saint Jacques, 15000 Besancon, France) *Med Biol Environ* 4(1): 64-65; 1976.

Larvae of the mosquito *Aedes aegypti*, known to be a carrier of Epstein-Barr virus, were cultured and infected with VT4 virus, an oncogenic virus that produces reticulosarcomas in chloramphenicol-inoculated Swiss mice. The larvae developed much faster in medium enriched with a casein hydrolysate than in medium enriched with yeast extracts. The larva cultures were inoculated with a cell-free extract obtained from spleen homogenates of Swiss mice infected with VT4. After 24 hr, the cultures, after being washed several times, were injected ip into 10 adult Swiss mice. The mice developed reticulosarcomas and splenomegaly in about 4 wk. (3 refs.)

77-4539 **Altered Sensitivity to Animal Virus as a Phenotypical Expression of the Oncogenic**

Transformation of Human Cells (Meeting Abstract). (Ita.) Valensin, P. E. (Istituto di Microbiologia, Universita di Siena, Siena, Italy) Bianchi Bandinelli, M. L.; Pellegrini, V.; Cellesi, C. *Ann Sclavo* 18(6): 882-883; 1977. (no refs.)

77-4540 **Morphological Transformation of Rat Embryonic Fibroblasts by Abortive Herpes Simplex Virus Infection: Increased Transformation Rate Correlated to a Defective Viral Genotype.** (Eng.) Schroder, C. H. (Inst. Virus Res., German Cancer Res. Center, Heidelberg, W. Germany) Kaerner, H. C.; Munk, K.; Darai, G. *Intervirology* 8(3): 164-171; 1977.

The presence of a defective viral genotype in rat embryo fibroblasts was correlated with an increased incidence of transformation in cells abortively infected with herpes simplex virus type 1 strain ANG at 42 C. The survival of these cells could depend on changes in the population of defective genotypes as well as on the quantity of defective virions. (20 refs.)

77-4541 **Studies on the Intracellular Replicating DNA of Herpes Simplex Virus Type 1.** (Eng.) Hirsch, I. (Inst. Sera and Vaccines, Dept. Experimental Virology, Praha, Czechoslovakia) Cabral, G.; Patterson, M.; Biswal, N. *Virology* 81(1): 48-61; 1977.

Analysis of intracellular replicating molecules of herpes simplex virus type 1 (HSV-1) DNA by restriction endonucleases and electron microscopy revealed the presence of internal replication loops and lariat-type molecules. The origin and function of the lariat molecules are not known; however, the results suggest that the origin of HSV-1 DNA synthesis is located in the joint region of the S arm of the molecule. (27 refs.)

77-4542 **Ribonucleotide Reductase from Herpes Simplex Virus (Types 1 and 2) Infected and Uninfected KB Cells: Properties of the Partially Purified Enzymes.** (Eng.) Ponce de Leon, M. (Dept. Microbiology Sch. Dental Medicine, Univ. Pennsylvania, Philadelphia, PA 19174) Eisenberg, R. J.; Cohen, G. H. *J Gen Virol* 36(1): 163-173; 1977.

The properties of partially purified ribonucleotide reductase (RR) from uninfected KB cells were compared with those of RR obtained from KB cells infected with herpes simplex virus (HSV) types 1 or 2; RR plays a critical role in the control of DNA synthesis. HSV-induced RR differed from the host enzyme in three respects: (1) it was not significantly inhibited by deoxyribonucleoside triphosphate, regardless of ATP concentration; (2) it did not require magnesium for activity, although 2 mM $Mg^{2}+$ did stimulate the reaction; (3) the magnesium concentration required for optimal activity was different for the virus and host enzymes. The virus enzymes were inhibited markedly by 5 mM $Mg^{2}+$ concentration for KB cell reductase. It is concluded that the RR enzyme molecules present after infection by HSV-1 or HSV-2 differ from those present before infection. (31 refs.)

77-4543 **Biophysical and Biochemical Alterations in the Surface of Herpes Simplex Virus Infected Cells (Meeting Abstract).** (Eng.) Thompson, C. J. (Pennsylvania State Univ., University Park, PA 16802) *Diss Abstr Int [B]* 38(2): 523; 1977. (no refs.)

77-4544 **Chemical Structure of Attachment Sites for Viruses on Human Erythrocytes.** (Eng.) Enegren, B. J. (Dept. Medical Biology, C. W. Post Coll., Greenvale, NY) Burness, A. T. *Nature* 268(5620): 536-537; 1977.

Evidence is presented that glycophorin is a human RBC receptor for encephalomyocarditis (EMC) virus. The binding site for both EMC and influenza virus on glycophorin is tentatively identified as three sialic acid residues remaining with the cells after trypsinization. (8 refs.)

77-4545 **Persistence of Type 5 Adenovirus DNA in Cells Transformed by a Temperature-sensitive Mutant, H5ts125.** (Eng.) Mayer, A. J. (Dept. Genetics, Albert Einstein Coll. Medicine, Bronx, NY 10461) Ginsberg, H. S. *Proc Natl Acad Sci USA* 74(2): 785-788; 1977.

H5ts125, a temperature-sensitive, DNA-minus mutant of adenovirus type 5, transforms three to eight times more embryo cells than wild-type adenovirus 5. This property was correlated with the persistence of an increased proportion of the viral genome in cells independently transformed at the nonpermissive (39.5 C) or semipermissive (36 C) temperature. Reassociation kinetics of the hybridization of ^{32}P-labeled, *Hin*dIII restriction fragments of the viral genome and excess unlabeled, transformed cell DNA was used to measure the quantity of the viral genome in transformed cells. Three of four cell lines independently transformed and maintained at 36 C contained all regions of the viral genome, one line transformed at 39.5 C contained multiple copies representing all of the viral DNA, and one line contained a large proportion of the viral genome. The cell line transformed and maintained at 32 C contained the viral genome in an amount consistent with that usually found in cells transformed by wild-type 5 adenovirus. The data suggest that a virus-specific DNA-binding protein, the "125 gene" product, may regulate viral transformation. (26 refs.)

77-4546 **Effect of BCG Vaccine on Adenovirus-induced Transplantable Tumor in Hamsters.** (Bul.) Silianovska, K. (Medical Acad., Inst. Oncology, Bulgaria) Boeva, M.; Nedialkova, M. *Onkologiia* 13(4): 172-175; 1976.

The effect of BCG vaccine on the appearance and growth of transplantable tumors that originated from nondifferentiated sarcomas initially induced in hamsters by bovine adenovirus type 3 was studied. The vaccine had 2×10^7 live organisms in 10 mg/ml. There were 7 experimental groups, each containing 15 60-day-old hamsters. The first six groups received 10^7 tumor cells id. Groups 1 and 3 were inoculated with BCG (2×10^4 organisms) ip and id, respectively, 20 days before tumor transplant. Group 4 was inoculated ip with BCG on the day of the transplant, and Group 5 was inoculated with a mixture of BCG and tumor cells. When the tumor reached 0.5 cm^3, Groups 2, 3, and 4 received the vaccine intralesionally. Groups 6 (tumor cells only) and 7 (untreated) served as controls. The hamsters were observed for 45 days, and tumor appearance and rate of growth were measured twice weekly. Regardless of the method, BCG vaccine did not inhibit tumor growth. A parallel study of humoral and cell-dependent cytotoxicity by the ^{51}Cr cytotoxicity test showed only minor differences between the BCG-treated groups and Group 6. (15 refs.)

77-4547 **Identification and Characterization of Adenovirus Tumor Antigens (Meeting Abstract).** (Eng.) Levinson, A. D. (Princeton Univ., Princeton, NJ 08540) *Diss Abstr Int [B]* 38(2): 653; 1977. (no refs.)

77-4548 **Synthesis and Characterization of Low Molecular Weight RNA in Adenovirus Type 2 Infected KB Cells (Meeting Abstract).** (Eng.) Sehulster, L. M. (Rutgers Univ.-State Univ., New Brunswick, NJ 08903) *Diss Abstr Int [B]* 38(2): 523; 1977. (no refs.)

See also:
* (Rev.): 77-4201, 77-4204, 77-4232, 77-4233, 77-4235, 77-4236, 77-4237, 77-4239, 77-4252, 77-4253.
* (Chem.): 77-4309, 77-4326, 77-4343, 77-4458.
* (Phys.): 77-4469.
* (Immun.): 77-4571, 77-4572, 77-4573, 77-4574, 77-4575, 77-4576, 77-4577, 77-4586, 77-4587, 77-4588, 77-4592.
* (Path.): 77-4639, 77-4654, 77-4687, 77-4693, 77-4694.

77-4549 **Assay of Immune Cytolysis of Lymphocytes and Tumour Cells by Automatic Determination of Cell Volume Distribution.** (Eng.) Reif, A. E. (Boston City Hosp., Boston, MA 02118); Robinson, C. M.; Incze, J. S. *Immunology* 33(1): 69-80; 1977.

A new method for determining immune cytolysis was developed. It uses a Coulter multichannel particle size analyzer in conjunction with a Coulter counter to document changes in cell volume due to immune cytolysis. Tumors used were L1210 leukemia, Ehrlich ascites carcinoma, and sarcoma-180, which were transplanted ip in DBA/2J mice. DBA/2J thymus, spleen, and lymph node lymphocytes were used in single cell suspensions. Assay tubes contained 100,000 viable tumor cells or lymphocytes, absorbed guinea-pig complement, and serial doubling dilutions of antiserum. After incubation for 1 hr at 37 C, each tube was placed in ice water, and trypsin or pronase was added. Cells were resuspended, a buffered electrolyte soln was added, and the suspension was decanted into cuvette. The cuvette was placed in the counter, and cell volume was analyzed and the accumulated cell volume distribution was plotted. For Ehrlich ascites and sarcoma-180 cells, volume degradation corresponding to vital staining was obtained only if trypsin (final concentration 625 μg/ml) was added immediately after the 1-hr incubation. For L1210 leukemia cells, trypsin was added at 0 C, 1 min before evaluation, to avoid potentiation of antibody-mediated cell lysis by trypsin. Immune cytolysis of the lymphocytes required addition of pronase (final concentration 625 μg/ml) at 0 C for further disruption of antibody-damaged cells prior to determination of cell volume distribution. Scanning electron micrographs of L1210 cells undergoing immune cytolysis illustrated the changes in cell volume recorded by the Coulter apparatus. This new method provides detailed information about the volume distribution of target cells and gives insight into the process of cytolysis. (22 refs.)

77-4550 **F_1 Hybrid Antiparental Cell-mediated Lympholysis: A Comparison with Bone Marrow Graft Rejection and with Cell-mediated Lympholysis to Alloantigens.** (Eng.) Shearer, G. M. (Immunology Branch, NCI, Bethesda, MD 20014); Cudkowicz, G.; Schmitt-Verhulst, A. M.; Rehn, T. G.; Waksal, H.; Evans, P. D. *Cold Spring Harbor Symp Quant biol* 41: 511-518; 1977.

General criteria for comparing the generation of F_1 antiparent cytotoxicity in vitro to both bone marrow graft rejection in vivo and the generation of allogenic cytotoxicity in vitro are considered. Four positive correlations have been demonstrated between hemopoietic graft rejection in vivo and F_1 antiparent cell-mediated cytotoxicity (CML) in vitro: genetic polymorphism, immunologic maturation, antigen-induced specific unresponsiveness, and selective but nonspecific abrogation of responsiveness, either by antisera or antimacrophage agents. The observations that F_1 antiparent cytotoxic potential develops later than immunity to alloantigens and that selective abolition of F_1 antiparent cytotoxicity can be achieved without abrogation of reactivity to alloantigens suggest that these two cell-mediated immune phenomena may be generated by different mechanisms and that common mechanisms may exist between the rejection of parental bone marrow grafts by irradiated F_1 mice in vivo and the generation of F_1 antiparent cytotoxicity. The lack of correlation between these same four criteria applied to F_1 antiparent CML in vitro and allogenic CML in vitro indicates that significant differences must exist between the two CML reactions. The most likely interpretation is that (1) the antigenic determinants and the genes controlling antigenic expression differ in the Hh and allogenic systems and (2) marrow graft rejection in irradiated hosts in vivo and the generation of Hh-specific cytotoxic effector cells are effected by different cellular mechanisms, although certain aspects of the cellular events in both systems are common. The F_1 antiparent cytotoxic model may be of value in typing and matching prospective marrow donors and recipients. (23 refs.)

77-4551 **Growth of Human Tumors in Lethally Irradiated Mice Reconstituted with Syngeneic Fetal Liver Cells.** (Eng.) Saltzstein, E. C. (Dept. Surgery, Mount Sinai Medical Center, 950 N. 12th St., Post Office Box 342, Milwaukee, WI 53201) Rose, W. C.; Truitt, R. L.; Rimm, A. A.; Bortin, M. M.; Patillo, R. A. *Cancer* 39(2): 581-586; 1977.

A model system is presented for xenografting human tumor cell lines into lethally irradiated (950 rads midline at a rate of 119 rads/min), fetal liver-reconstituted A and CBA mice. At 24 hr after irradiation, the mice were inoculated iv with 2 x 10^7 fetal liver cells from syngeneic donors (14, 16, or 18 days of embryonation) and sc with 1, 3, or 6 x 10^6 human choriocarcinoma (C-1, C-2, and C-3) or human breast carcinoma (B-1) cells. Palpable tumors $\geqslant$ 5 mm were found in 55/78 mice: 18/22 with C-1, 9/16 with C-2, 10/10 with C-3, and 18/30 with B-1. Evidence for successful engraftment was based on the histologic appearance of the neoplastic tissue, metastatic pulmonary lesions, and, in mice that received transplants of choriocarcinoma cells, the appearance of human chorionic gonadotropin in their serum. Tumors of 17/55 mice grew progressively until death or until the mice were sacrificed at 100 days postinoculation. (32 refs.)

77-4552 **Reactions of the Tumour Bed to Lethally Irradiated Tumour Cells, and the Revesz Effect.**

Eng.) Van den Brenk, H. A. (Richard Dimbleby Dept. Can-
er Res., St. Thomas's Hosp. Medical Sch., London SE1
EH, England) Crowe, M. C.; Stone, M. G. *Br J Cancer*
6(1): 94-104; 1977.

ubdermal inoculation of the foot of female Carworth Farm
ats with lethally irradiated (LI) W256 Walker tumor cells
nixed with viable (V) W256 cells decreased the latent period
or initiation of allogeneic tumor growth without significantly
ffecting its rate. This Revesz effect decreased with increase
n the number of inoculated V cells and with decrease in age
f the recipient. LI cells of Y-P388 Yoshida rat tumor exerted
Revesz effect, even in recipients immunized with LI Y-P388
umor cells. Local preirradiation of the inoculation site of V
ells decreased both the latent period and tumor growth rate.
t acted independently of a Revesz effect, and the decrease
n tumor growth rate was partly due to emigration of V cells
rom the inoculum, producing metastases. LI, but not heat-
illed cells, induced prolonged swelling of the tumor bed in
nimmunized and tumor-immunized rats, which, unlike in-
lammatory swelling, was inhibited by preirradiation of the
oot. It is postulated that the Revesz effect is due to enhance-
nent of survival of V cells by trophic substances that are
rincipally elaborated by LI (and V) cells and also by the
umor bed due to innate growth and the trophic reactions of
he tissues to the presence of tumor cells. (16 refs.)

7-4553 **Lung Colony Assay in Normal, Irradiated and
Tumor Bearing Mice.** (Eng.) Janik, P. (Dept.
'umor Biology, Inst. Oncology, 00 973, Warszaw, Poland)
Veoplasma 23(5): 495-497; 1977.

xperiments were performed to determine whether im-
nunosuppression or the tumor process itself facilitates the
akes of clonogenic cells in BALB/c mice injected iv with
yngeneic lung tumor cells (0.5 x 10^6, 0.25 x 10^6, or 0.125 x
0^6 cells). The recipient animals were normal mice, mice sub-
ected to whole-body x-irradiation (300 R) 1 day prior to iv
nplantation, or mice bearing sc implants of the same tumor.
lung colony assay performed 1 mo after the tumor cell
njection showed that both irradiated and tumor-bearing
nice developed many more metastases than the normal
nimals. In all three groups, the number of lung colonies
lepended on the number of tumor cells injected. (7
efs.)

7-4554 **Non-specific Cytotoxicity of Spleen Cells in
Mice Bearing Transplanted Chemically Induced
'ibrosarcomas.** (Eng.) Mantovani, A. (Istituto di Ricerche
'armacologiche "Mario Negri," Via Eritrea 62, 20157 Milan,
taly) Evans, R.; Alexander, P. *Br J Cancer* 36(1): 35-40;
977.

pleen cells from CBA and C57BL mice bearing transplanted chemically induced syngeneic fibrosarcomas nonspecifically inhibited DNA synthesis of sarcoma and lymphoma target cells in vitro. Splenocytes from mice hyperimmunized against a syngeneic sarcoma specifically inhibited DNA synthesis of the tumor used for immunization. The impairment of tumor cell DNA synthesis was associated in vitro with cytostasis, and lysis of the target cells was not seen. Since treatment with anti-θ serum and complement did not impair the cytostatic action of the spleen cells and since thymus-deprived animals showed similar activity to normal mice, T lymphocytes were not involved in nonspecific cytostasis. Removal of phagocytic adherent cells by carbonyl iron markedly inhibited the cytostatic activity of the spleen cells, suggesting a role in this reaction for cells of the monocyte-macrophage series. The presence of an actively growing sarcoma was a prerequisite for the expression of nonspecific cytostasis, since surgical excision resulted in complete disappearance of this spleen cell activity. (16 refs.)

77-4555 **Natural Cytotoxic Cells Against Solid Tumors in Mice (Meeting Abstract).** (Eng.) Stutman, O. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021) Paige, C.; Cuttito, M.; Cahan, A.; Figarella, E. F. *Proc Am Assoc Cancer Res* 18: 247; 1977. (no refs.)

77-4556 **Recent Studies on Immune Reactions to Chemically Induced Mouse Tumors (Meeting Abstract).** (Eng.) Hellstrom, I. (Fred Hutchinson Cancer Res. Center, Seattle, WA) Brown, J.; Hellstrom, K. E.; Klitzman, J.; Nepom, J.; Nowinski, R. *J Reticuloendothel Soc* 22(2): 96-97; 1977. (no refs.)

77-4557 **Effect of Sera from Mice with Sarcomas Induced by Methylcholanthrene on the Reimplantation and Cell Growth of Syngeneic Tumors.** (Ukr.) Kamins'ka, L. P. (Inst. Oncology Problems, Acad. Sciences, Ukrainian SSR, USSR) *Dopov Akad Nauk Ukr RSR Ser B* (4): 338-341; 1977.

A transplantation test was used on irradiated mice to study the presence of a blocking factor and the inhibition or acceleration of tumor growth in 3-methylcholanthrene (MC)-induced sarcomas incubated in autologous sera. Sera were obtained from the mice at various times after the administration of MC. In 2/4 series of experiments on BALB/c mice, the sera of healthy animals had a cytotoxic effect. The tumor size was 1.6-2 times smaller than in control mice (those with sarcomas but without serum treatment) but sera from MC-treated mice accelerated tumor growth. In other experiments, only sera obtained during max development of the blastoma stimulated tumor growth. In 2/3 series of experiments on

C57BL mice, sera from healthy animals inhibited tumor cell transplantation. The blastoma was 2-3 times smaller than that in controls. Sera from MC-treated mice did not affect the tumor cell consistently, which may be a result of the course of the blastoma development induced by the carcinogen. The high cytotoxicity of the sera of healthy mice decreased during the experiment. Differences in the effect of the serum on autologous tumor cells may be related to differences in the humoral reaction of the mice to tumor induction. (9 refs.)

77-4558 **Castration Effects on Tumor Specific Immunity.** (Eng.) Brannen, G. E. (Box 871, Urology Service, Madigan Army Medical Center, Tacoma, WA 98431) Gomolka, D. M.; Wettlaufer, J. N.; Modarelli, R. O. *Invest Urol* 15(1): 28-38; 1977.

This two-part study was conducted to determine the effects that orchiectomy might have on tumor-specific transplantation immunity. Using two immunogenic 3-methylcholanthrene (MCA)-induced murine fibrosarcomas, in male $CD2F_1$ mice, (1) growth rates of the immunogenic sarcomas were compared in control and castrated mice and (2) tumor-specific resistance to challenge with graded doses of tumor cells was compared in castrated and noncastrated mice immunized to the challenging tumor line. The fibrosarcomas, MCAM-3 and MCAM-7, were induced by sc injection of 2 mg MCA in 0.01 ml trioctanoin. In the first experiment, using MCAM-3, a significant increase (over controls) in tumor size and mortality occurred in castrated mice 30 days after tumor transfer. Using MCAM-7, a significant increase in tumor size occurred, in castrated mice only, from days 14 to 26 after transfer. However, mortality increased after day 26. In the second experiment, without exception, control mice showed more rapid tumor growth and higher mortality than MCAM-immunized mice. These findings were constant with either MCAM-3 or MCAM-7, regardless of challenge dose of tumor cells. In no instances did mice that were castrated and immunized to either tumor differ from noncastrated immunized mice regarding tumor growth or mortality. Thus, castration had no observable effects on tumor-specific immunoresistance. Mechanisms of host-tumor immunorelationships are discussed. (40 refs.)

77-4559 **The Effect of Pregnancy on the Growth of Primary Methylcholanthrene Sarcoma Isografts.** (Eng.) McLaughlin, A. P. (Scripps Memorial Hosp., 9844 Genesee Ave., La Jolla, CA 92037); Effron, M. K. *J Surg Oncol* 9(2): 107-110; 1977.

The incidence of tumor growth with methylcholanthrene fibrosarcoma isografts was significantly enhanced in both intra- and interstrain pregnant C57/BL mice compared to virgin C57/BL mice preimmunized with fetal antigens. Active preimmunization of virgin mice with hybrid fetal liver did not result in rejection of primary tumor isografts, which suggests that fetal antigens do not contribute to the immunogenicity of this tumor. (26 refs.)

77-4560 **Brief Communication: Yolk Sac Carcinoma Grown from Rat Egg Cylinders.** (Eng.) Damjanov, I. (Dept. Pathology, Univ. Connecticut Sch. Medicine, Farmington, CT 06032); Sell, S. *J Natl Cancer Inst* 58(5): 1523-1525; 1977.

Eight-day rat egg cylinders were transplanted under the kidney capsules of adult histocompatible recipients, giving rise to small nodules composed of parietal yolk sac cells surrounded by Reichert's membranelike material. These cells could grow and give rise to malignant, transplantable tumors identical to mouse yolk sac carcinomas derived from teratocarcinoma. (14 refs.)

77-4561 **48 Serially Transplanted Human Tumors in Nude Mice (Meeting Abstract).** (Eng.) Fogh, J. (Sloan-Kettering Inst. for Cancer Res., New York, NY 10021) Fogh, J. M.; Sharkey, F. E.; Hajdu, S. I.; Fitzgerald, P. J. *Proc Am Assoc Cancer Res* 18: 183; 1977. (no refs.)

77-4562 **Human Cancer and Other Transplants in the "Nude" Mouse.** (Eng.) Wynn-Williams, A. (Hamilton General Hosp., Hamilton, Ontario, Canada) McCulloch, P. *J Pathol* 122(4): 225-228; 1977.

Transplantation studies conducted with nude mice (Balb/c nu/nu) showed that xenografts of human tumors often grew successfully, that there was very little growth in allografts of actively growing normal tissue from Swiss mice, and that transplants of mature tissue from the toad failed to grow. (4 refs.)

77-4563 **Resistance to a Transplantable Rat Mammary Tumor (DMBA 8BT) After Pre Treatment with Fetal Cells (Meeting Abstract).** (Eng.) Kellen, J. A. (Dept. Clinical biochemistry, Sunnybrook Medical Centre, Toronto, Canada) Cocuzzi, E. *Proc Am Assoc Cancer Res* 18: 10; 1977. (no refs.)

77-4564 **Genetic Resistance to Bone Marrow Transplantation as a Leukemia Defense Mechanism: Possible Identity of M and NK Cells (Meeting Abstract).** (Eng.) Trentin, J. J. (Div. Experimental Biology, Baylor Coll. Medicine, Houston, TX 77030) Gallagher, M. T. *Proc Am Assoc Cancer Res* 18: 106; 1977. (3 refs.)

77-4565 **Resistance of Germfree Athymic Nude Mice to Two-Stage Epidermal Carcinogenesis (Meeting Abstract).** (Eng.) Holland, J. M. (Oak Ridge Natl. Lab., Oak Ridge, TN 37830) Perkins, E. H.; Gipson, L. C. *Proc Am Assoc Cancer Res* 18: 10; 1977. (no refs.)

77-4566 **Suppression of Babesiosis in BCG-infected Mice and Its Correlation with Tumor Inhibition.** (Eng.) Clark, I. A. (Microbiology Dept., John Curtin Sch. Medical Res., Canberra, Australia) Wills, E. J.; Richmond, J. E.; Allison, A. C. *Infect Immun* 17(2): 430-438; 1977.

Infection of CBA/Ca mice with *Mycobacterium bovis* strain BCG protected them from infection with *Babesia microti* and *B. rodhaini* and from the high parasitemia and death due to *Plasmodium vinckei.* A nonspecific soluble effector substance is the best explanation for this protection. (35 refs.)

77-4567 **Suppression of Mammary Tumorigenesis in C3H/He Mice by Variectomy or Treatment with 2-Bromo-α-ergocryptine: A Comparison.** (Eng.) Welsch, C. W. (Dept. Anatomy, Michigan State Univ., East Lansing, MI 48824) Lambrecht, L. K.; Hassett, C. C. *J Natl Cancer Inst* 58(4): 1135-1138; 1977.

The effects of chronic treatment with 2-bromo-α-ergocryptine (CB-154) and of ovariectomy on the genesis of mammary hyperplastic nodules (HN) and mammary tumors in the C3H/He mouse were compared. CB-154 is an established potent suppressor of pituitary prolactin. Eighty-five 21- to 25-day-old female mice were divided into three groups. Group I received daily sc injections of 0.1 mg CB-154, Group II was ovariectomized, and Group III served as controls. Mice were examined weekly for mammary tumors. Fifteen months from the onset of treatment all surviving mice were killed. The mean number of HN per inguinal mammary gland, total number of mammary tumors, and number of mice with mammary tumors in each group were, respectively: Group III, 46, 41, 24/29; Group II, 1.2, 20, 14/28; Group I, 0.2, 16, 13/28. A significant and equally comparable inhibition of mammary tumor incidence was observed in the ovariectomized and CB-154-treated mice. Thus, early ovariectomy and CB-154 treatment (specific inhibition of prolactin secretion) were equally effective in the prophylaxis of mammary tumorigenesis in the C3H/He female mouse. (19 refs.)

77-4568 **Immunization by the Intestinal Route of C3H-Mice Against C3H-L-Ascites Tumor Cells.** (Eng.) Laursen, M. L. (Fibiger Lab., Ndr. Frihavnsgade 70, DK-2100 Copenhagen 0, Denmark) Laursen, K. *Proc Soc Exp Biol Med* 154(2): 314-317; 1977.

An investigation was made to determine whether the intracecal (ic) administration of live syngeneic tumor cells can protect against subsequent challenge by the same tumor cells administered ip. When C3H/Fib mice were inoculated with 10^7 C3H-L 1/a tumor cells (derived from a spontaneous in vitro transformation of C3H lung fibroblasts), 16/21 died from resulting tumors. Only 1/18 and 1/20 similarly challenged mice succumbed to tumors when inoculated ic with 10^7 tumor cells either 8 or 26 days beforehand, respectively. The immunizing properties of the ic inoculated cells were further demonstrated by the presence of specific antibodies in the treated mice, as evidenced by a positive indirect immunofluorescence test. The protective effect could be transferred to untreated animals by sensitized splenocytes. Frozen and thawed cells administered ic were not effective at protecting against subsequent challenge. (11 refs.)

77-4569 **Enhanced Immunogenicity in Syngeneic Hosts of Lymphoma Cells Modified to Increase Lipophilicity (Meeting Abstract).** (Eng.) Prager, M. D. (Univ. Texas Health Science Center, Dallas, TX 75235) Gordon, W. C. *Proc Am Assoc Cancer Res* 18: 30; 1977. (no refs.)

77-4570 **Changes in the Immunologic Status Reflected in the Physicochemical Characteristics of Cells of the Immunocompetent System During Carcinogenesis.** (Eng.) Stepanova, E. N. (Scientific-Res. Lab. Experimental Immunobiology, Acad. Medical Sciences USSR, Moscow, USSR); Airapet'yan, G. P.; Maiskii, I. N. *Bull Exp Biol Med* 83(1): 85-88; 1977.

Cells obtained from the lymph nodes and thymus of male Wistar rats bearing 9,10-dimethyl-1,2-benzanthracene-induced sarcomas of the thigh were studied by immunofluorescence. Statistically significant changes in the uptake of aniline-8-naphthaline sulfonate in cell suspensions depended on the stage of development of the sarcoma. (10 refs.)

77-4571 **Inhibition of Murine RNA Tumor Virus Expression and Tumorigenesis by Polyadenylic Acids.** (Eng.) Tennant, R. W. *In: Modulation of Host Immune Resistance in the Prevention or Treatment of Induced Neoplasias. NCI and John E. Fogarty International Center for Advanced Study in the Health Sciences. (Bethesda, Maryland):* pp. 157-162; 1974.

The effect of polyadenylic acids [poly(A)] on the expression of murine RNA tumor viruses was examined. In vivo poly-2′-O-methyladenylic acid [poly(Am)] was effective against tumorigenesis by Moloney sarcoma virus Poly(Am) increased the humoral antibody response of mice to RNA tumor virus antigens and their immune response to sheep RBC. A single 10-μg dose of poly(Am) 4 hr prior to virus inoculation produced long-term protection against tumor induction and death. In cell culture, poly(Am) or poly(A) (10 μg/ml) inhibited exogenous virus infection when added within a few hours after the virus, and they inhibited cell transformation. At 100 μg/ml, the compounds inhibited the adsorption of RNA tumor virus but not Sindbis virus, and poly(A) was less effective than poly(Am). In vitro, the effect was related to the competitive inhibition of viral reverse transcriptase by poly(Am) or poly(A). The influence of poly(Am) in vivo seems to be related primarily to an interaction with immune functions of the host rather than action against some viral functions, as in the cell culture and in vitro systems. (17 refs.)

77-4572 **Natural Immunity in Mice to the Envelope Glycoprotein of Endogenous Ecotropic Type C Viruses: Neutralization of Virus Infectivity.** (Eng.) Ihle, J. N. (Basic Res. Program, NCI Frederick Cancer Res. Center, Frederick, MD 21701) Lazar, B. *J Virol* 21(3): 974-980; 1977.

The ability of naturally immune mouse sera to neutralize ecotropic AKR murine leukemia virus (MuLV) was examined using unfrozen virus preparations harvested for 1 hr. In this assay, several mouse sera significantly and consistently neutralized MuLV infectivity. This ability was correlated with the presence of MuLV antibodies that were detectable in a radioimmune precipitation assay with radiolabeled intact virions. This neutralization was specific: either N- or B-tropic viruses but not Friend MuLV were neutralized. Neutralization could be abrogated with purified AKR MuLV gp71 at concentrations that do not interfere with virus infectivity, but it could not be abrogated with Rauscher MuLV gp71. Neutralizing activity was removed by absorption with intact AKR MuLV, but not by absorption with Friend MuLV, BALB/c xenotropic virus, or NZB xenotropic virus. All the neutralizing activity of $(B6C3)F_1$ mouse sera was associated with the IgG fraction. (30 refs.)

77-4573 **Cellular Immunity Against Rous Sarcomas (Meeting Abstract).** (Eng.) Wainberg, M. A. (Lady Davis Inst. Medical Res., Montreal, Canada) Schwartz-Luft, E.; Israel, E. *Proc Am Assoc Cancer Res* 18: 36; 1977. (no refs.)

77-4574 **Cellular Immune Response to Herpes Virus Antigens in Patients with Cervical Carcinoma (Meeting Abstract).** (Eng.) Kumar, A. (Case Western Reserve Univ. Sch. Medicine at Cleveland Metropolitan General Hosp., Cleveland, OH 44109) Selim, M. A.; Vasquez, H. H.; Nankervis, G. A. *Proc Am Assoc Cancer Res* 18: 72; 1977. (no refs.)

77-4575 **IgG-, IgA- and IgM-Antibodies to Herpes Simplex Virus Type 2 in Sera from Patients with Cancer of the Uterine Cervix.** (Eng.) El Falaky, I. H. (Inst. Medical Microbiology, Univ. Copenhagen, 22 Juliane Maries Vej, DK-210 Copenhagen 0, Denmark) Vestergaard, B. F. *Eur J Cancer* 13(3): 247-251; 1977.

Sera from 60 patients with cervical cancer, 60 matched controls, and 13 patients (22 samples) with recent herpes genitalis were examined by the indirect fluorescent antibody method for the presence of IgG, IgA and IgM antibodies to herpes simplex virus (HSV) type 2. IgG antibody titers in the patients with cervical cancer were significantly higher than those found in the control group, but IgA and IgM antibodies were normal. All three immunoglobulins were elevated in the patients with frequent recurrent HSV-2 infections. The elevation of a single class of immunoglobulin to HSV-2 infection is serologically unusual and distinguishes patients with cervical cancer not only from normal controls, but also from patients with frequent recurrent or chronic genital herpes. (15 refs.)

77-4576 **Immunoelectron Microscopic Studies with Sera from Patients with Prostatic Neoplasia and Type C Virus Producing Mouse Prostate Culture Cells (Meeting Abstract).** (Eng.) Ohtsuki, Y. (Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX 77030) Dmochowski, L.; Seman, G.; Bowen, J. M.; Johnson, D. E. *Proc Am Assoc Cancer Res* 18: 207; 1977. (no refs.)

77-4577 **Effects of Lymphocytes from Marek's Disease-infected Chickens on Mitogen Responses of Syngeneic Normal Chicken Spleen Cells.** (Eng.) Theis, G. A. (Dept. Pathology, New York Medical Coll., Valhalla, NY 10595). *J Immunol* 118(3): 887-894; 1977.

The response to phytohemagglutinin was measured in mixed lymphocyte cultures of cells from normal chicken spleens and spleen or thymus cells from syngeneic chickens infected with Marek's disease virus (MDV). MDV spleen cells from tumor bearing chickens exerted a suppressive effect on normal spleen cell response. (39 refs.)

77-4578 **Lymphoma Susceptibility of the θ-C3H ARK/Cum.** (Eng.) Tuffrey, M. A. (Dept. Embryology and Foetal Development, Clinical Res. Centre, Watford Road, Harrow, Middlesex, England); Crewe, P.; Dawson, L. *Br J Cancer* 35(3): 376-377; 1977.

One of the two θ-C3H sublines of the AKR strain of mice, AKR/Cum, was examined for the incidence of lymphoma and compared with the θ-AKR lymphoma-susceptible AKR/J mice to learn of any possible association between lymphoma susceptibility and θ status. The results indicate no such association. (4 refs.)

77-4579 **Immune Reactivity in Regional Lymph Nodes in Squamous Head and Neck Cancer (Meeting Abstract).** (Eng.) Saxon, A. (Dept. Microbiology and Immunology, UCLA Sch. Medicine, Los Angeles, CA 90024) Portaro, J. *Proc Am Assoc Cancer Res* 18: 51; 1977. (no refs.)

77-4580 **Comparison of Immune Reactivity of Various Lymphocyte Populations Against Experimental or Spontaneous Tumors (Meeting Abstract).** (Eng.) McWilliams, R. W. (FCRC, Frederick, MD 21701) *Proc Am Assoc Cancer Res* 18: 9; 1977. (no refs.)

77-4581 **Concomitant Presence of Tumor-specific Cytotoxic and Inhibitor Lymphocytes in Patients with Osteogenic Sarcoma.** (Eng.) Yu, A. (Dept. Immunology, Children's Hosp. Medical Center, Boston, MA 02115); Watts, H.; Jaffe, N.; Parkman, R. *N Engl J Med* 297(3): 121-127; 1977.

Evidence is presented that the peripheral blood lymphocytes (PBL) of osteogenic sarcoma patients that do not have detectable in vitro tumor-specific cytotoxicity (TSC) contain a subpopulation of lymphocytes that mediate TSC and a second subpopulation that inhibits the in vitro cytotoxicity of the first. Three osteogenic sarcoma tissue culture lines were used as target cells, and unfractionated PBL were obtained from 28 osteogenic sarcoma patients. PBL from 12 of the patients demonstrated significant ($p < 0.001$) tumor cytotoxicity against the target cells. Seven of these 12 patients did not have concomitant cytotoxicity to control fibroblasts or melanoma cells. When the PBL from 13 patients whose lymphocytes were not cytotoxic underwent fractionation, a subpopulation showing TSC was isolated from 11 patients. Lymphocytes that inhibited the cytotoxicity of autologous tumor-specific cytotoxic lymphocytes were found in 4/10 patients but not in 6 controls. The inhibitor lymphocytes form rosettes with sheep RBC and adhere to nylon; the cytotoxic lymphocytes have a receptor for C3 but no surface immunoglobulin. Thus, the lack of TSC in some patients can be due to inhibitor lymphocytes. The cell responsible for tumor cytotoxicity is a medium-density lymphocyte whose surface characteristics differ from those of mature T or B lymphocytes. The inhibitor lymphocyte is a T lymphocyte with a lighter density. (25 refs.)

77-4582 **Lack of Correlation of Activated Monocytes with Lymphocyte Function in Patients with Lymphoma.** (Eng.) Sagone, A. L. (Univ. Hosp. N-1027, 410 W. Tenth Ave., Columbus, OH 43210) Kamps, S.; Campbell, R.; King, G. W. *J Reticuloendothel Soc* 21(6): 377-383; 1977.

The relation between monocyte and lymphocyte function was studied in 10 male patients with biopsy-proved lymphoma, Stages I, II, and IV. Glucose metabolism was studied as a measure of monocyte activation, and lymphocyte function was estimated by the response of these cells to nonspecific mitogens: phytohemagglutinin (PHA) and pokeweed mitogen (PWM). Glucose utilization and $^{14}CO_2$ production from ^{14}C-1-glucose and ^{14}C-6-glucose were determined for the monocyte monolayers during 24 hr of incubation. The patients fell into two groups on the basis of normal or impaired lymphoblastic transformation to PHA. Group I cultures had ^{3}H-thymidine uptakes similar to those of normal subjects, and they were from four patients with Hodgkin's disease and one with non-Hodgkin's lymphoma. The PWM cultures of four of these patients had normal uptakes and one was impaired. The lymphocyte cultures of 4/5 patients in Group II had thymidine uptakes well below normal; the fifth culture had an uptake at the lower limits of normal. Transformation of the PWM cultures of all these patients was impaired. Glucose metabolism of the monocytes of 5/10 patients was enhanced, as indicated by higher rates of glucose utilization or ^{14}C-1-glucose oxidation. However, activated monocytes were present in 2/5 Group I patients and in 3/5 Group II patients. Thus, enhanced monocyte metabolism did not correlate with lymphoblastic transformation, which suggests that the activation of monocytes in vivo may not depend on lymphocyte factors. (29 refs.)

77-4583 **Phenotypic Characterization of a Unique Non-T, Non-B Acute Lymphoblastic Leukaemia Cell**

Line. (Eng.) Rosenfeld, C. (Institut de Cancerologie et d'Immunogenetique, INSERM, 16, Ave. Paul Vaillant Couturier, Villejuif, France) Goutner, A.; Choquet, C.; Venuat, A. M.; Kayibanda, B.; Pico, J. L.; Greaves, M. F. *Nature* 267(5614): 841-843; 1977.

A lymphoid cell line (Reh) was established from the peripheral blood of a 15-yr-old girl in relapse from acute lymphocytic leukemia (ALL). The Reh cells contained no detectable Epstein-Barr virus. Fresh WBC preparations consisted of populations that were cytogenetically different, one normal (46, XX), the other abnormal (45, XX, -2B, +1C). Denaturation techniques suggested that the two missing B are one No. 4 and one No. 5 and that the extra C is not a true C, but probably a structural rearrangement. The Reh cells were able to proliferate at the beginning of the culture, and they overcame the cytogenetically normal population. The initial cells from the patient and those established in vitro were negative for sheep RBC rosette formation and surface immunoglobulin and were therefore considered to be of the null type. The phenotypic prolife of Reh was identical to that of the common form of ALL. The Reh cells were positive for membrane markers and enzyme assays unique to non-T, non-B ALL. Cell lines derived from the common form of lymphoblastic leukemia may be of value in investigations of the nature of leukemia-associated antigens and of the block to further differentiation that presumably exists in these cells. (33 refs.)

77-4584 **Immunologic Characterization of Chronic Lymphocytic Leukemia Cells.** (Eng.) Whiteside, T. L. (Dept. Pathology, Univ. Pittsburgh Sch. Medicine, Pittsburgh, PA 15261) Winkelstein, A.; Rabin, B. S. *Cancer* 39(3): 1109-1118; 1977.

Immunologic characterization of the circulating neoplastic lymphocytes of 21 patients with chronic lymphocytic leukemia (CLL) revealed significant differences in membrane characteristics from normal B lymphocytes. Although the leukemic cells bore homogenous membrane-associated immunoglobulin, they also reacted with an anti-human T-cell serum. In all patients studied, 69%-90% of the cells were stained by this antiserum. This suggests that the leukemic cells share antigenic determinants with T lymphocytes. CLL cells, unlike normal B cells, showed a marked increase in mouse-complement receptors. No increase in receptors for guinea pig complement was observed in the leukemic cells. The population of surface immunoglobulin-bearing lymphocytes was significantly greater than that of complement receptor-bearing lymphocytes. The total number of E-rosetting cells was increased in all CLL patients. Mitogenic responses of the leukemic cells were depressed and delayed. These results suggest that neoplastic lymphocytes cannot be classified as T- or B-derived on the basis of criteria used to define normal lymphocytes. (54 refs.)

77-4585 **Role of Normal Immunosuppressive Protei (NIP) in Immunologic Surveillance.** (Eng. Hanna, N. (Lil and Ben Stein Transplantation Lab., Dept Immunology, Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel) Ovadia, H.; Nelken, D. *Transplant Proc* 9(1) 1071-1073; 1977.

The effect of normal immunosuppressive protein (NIP) o (1) the in vitro induction of specifically cytotoxic T lymphocytes against tumor cells and (2) the antitumor cytotoxicity of sensitized T lymphocytes was investigated. NIP wa prepared by cold ethanol extraction of an α-globulin-ric fraction of human plasma. BALB/c mice were immunize against allogeneic C57BL EL-4 tumor cells by ip injection o 3 x 10^7 cells. Eleven days later, peritoneal exudate cells (PEC were harvested, and adherent cells were removed. The nonadherent PEC were highly cytotoxic against EL-4 target cells Preincubation of effector lymphocytes with various amount of NIP for 2 hr before addition of target cells had no effec on lymphocyte function. However, pretreatment with NI for 18 hr caused a strong and dose-dependent inhibition o lymphocyte cytotoxicity. Highest inhibition was observed a a lymphocyte:target cell ratio of 5:1 and at 4 mg NIP/ml Cytotoxicity was regenerated after a further 18-hr incubatio in the absence of NIP. NIP strongly suppressed the in vitr induction of allogeneic cytotoxic lymphocytes in both th proliferative and differentiative stages. Unlike the effect observed at the effector lymphocyte level, this suppression o induction was irreversible, and no cytotoxicity was observe after an 18-hr regeneration period. Minute amounts of NI (3.0 mg/3 x 10^6 cells/2.0 ml) were sufficient to suppress th induction of cytotoxic lymphocytes, but higher concentrations (4.0 mg/2 x 10^5 cells/0.5 ml) were needed to inhibi effector cell activity. (8 refs.)

77-4586 **The Role of T and Suppressor Cells in MTV-directed Cellular Immunity.** (Eng.) Creemers, P. (Radiobiological Institute TNO, Lange Kleiweg 151, Rijswijk, The Netherlands) Bentvelzen, P. *Eur J Cancer* 13(3): 261-267; 1977.

In BALB/cf C3H and GR mice immunized with mammary tumor virus (MTV), the lymphocyte populations that responded in vitro with blastogenesis in the presence of MTV proved to be T cells. In mice bearing spontaneous MTV-induced mammary tumors, this T cell reactivity was very often depressed. The depression was partly due to the presence of suppressor cells with adherent properties. These suppressor cells appeared early during tumor growth and exerted their greatest influence when tumor wt was 0.5-1.5g. Fewer suppressor cells were present in animals bearing large tumors; thus, other factors must also contribute to the depression of T-cell reactivity. (10 refs.)

77-4587 **Identification and Involvement of Hamster Thymus-Derived Lymphocytes in the Rejection f Syngeneic SV40- and Methylcholanthrene-induced Tumors (Meeting Abstract).** (Eng.) Blasecki, J. W. (Univ. Mis-issippi Medical Center, Jackson, MI 3916) *Proc Am Assoc Cancer Res* 18: 5; 1977. (no refs.)

77-4588 **An Immune Complex Assay for SV40 T Antigen.** (Eng.) Crawford, L. V. (Dept. Molecular Virology, Imperial Cancer Res. Fund, London WC2A 3PX, England) Lane, D. P. *Biochem Biophys Res Commun* 74(1): 323-329; 1977.

A direct immunoprecipitation assay is described for the detection of T antigen. With the appropriate sera, this assay may possibly be used to detect many other large antigens of biological interest. (15 refs.)

77-4589 **Immunogenicity of Human B Cell Antigens Solubilized from Cultured Human Lymphoid Cells.** (Eng.) Ferrone, S. (Dept. Molecular Immunology, Scripps Clinic and Res. Foundation, La Jolla, CA 92037); Pellegrino, M. A.; Reisfeld, R. A. *J Immunol* 118(3): 1036-1041; 1977.

Antigens solubilized from cultured human lymphoid cells were purified by ultracentrifugation on KBr gradients. In rabbits, these antigens generated lymphocytotoxic xenoantibodies which acquired specificity to B cells following absorption with melanoma cells. Xenoantisera reactions tested against peripheral B lymphocytes and chronic lymphocytic leukemia cells resembled those of alloantisera to B cell antigens. (34 refs.)

77-4590 **Mutations Affecting the Antigenic Properties of Hypoxanthine-Guanine Phosphoribosyl Transferase in Cultured Chinese Hamster Cells.** (Eng.) Fenwick, R. G. (Howard Hughes Lab. Study Genetic Diseases, Dept. Medicine, Baylor Coll. Medicine, Houston, TX 77030) Wasmuth, J. J.; Caskey, C. T. *Somatic Cell Genet* 3(2): 207-216; 1977.

As a study of forward and reverse mutation, HGPRT+ (hypoxanthine-guanine phosphoribosyl transferase) revertants were isolated from the mutant Chinese hamster cell line RJK10 (derived from V79 cells). This line is HGPRT- and does not contain any protein that cross-reacts immunologically with HGPRT. HGPRT from the revertant cells is less reactive with anti-HGPRT serum than HGPRT from V79 cells, and the enzymes from both sources are immunoprecipitated independently from mixtures of cell extracts. It is concluded that one or more of the antigenic determinants present on Chinese hamster HGPRT are either missing or present in an altered form on HGPRT from revertants of RJK10. This indicates that RJK10 carries a mutation in the structural gene for HGPRT and that secondary mutations in the gene give rise to the revertants that produce the antigenically altered HGPRT. (16 refs.)

77-4591 **Cell Surface Antigens in a Rat Colon Cancer Model: Correlation with Inhibition of Tumor Growth.** (Eng.) Steele, G. (Peter Bent Brigham Hosp., 721 Huntington Ave., Boston, MA 02115) Sjogren, H. O. *Surgery* 82(1): 164-169; 1977.

Tumor challenge isograft experiments were performed to determine the possible in vivo significance of the surface antigens associated with the intestinal adenocarcinomas induced in Wistar/Furth (W/F) rats by 1,2-dimethylhydrazine 3HCl (DMH) or N-methyl-N′-nitro-N-nitrosoguanidine (NG). W/F males in groups of 20 animals were inoculated sc with three immunizing doses of 10^7 cells from the chemically induced colon carcinomas NG-WI, DMH-W49, or DMH-W9 or the small-bowel adenocarcinoma DMH-W7. Control rats were immunized with a non-cross-reacting adenovirus- induced mammary fibroadenoma (49-W1). Six weeks after immunization, all animals were challenged with 1×10^5 or 3×10^4 colon carcinoma NG-W1 cells. None of the NG-W1-immunized animals developed tumors after either NG-W1 challenge dose. In contrast to this strong protection by a "private" tumor rejection antigen (TRA), protection by common or tissue type-specific antigens was evident only if tumor volumes were measured. Twenty-two days after low-dose NG-W1 challenge, mean tumor volumes (m) in animals immunized with DMH-W9 ($m = 0.25$ cm^3) and DMH-W49 ($m = 0.17$ cm^3) were less ($p < 0.05$) than in animals untreated ($m = 1.0$ cm^3) or immunized with A9-W1 ($m = 0.9$ cm^3). Embryonic antigens also may function as weak TRA's. NG-W1 challenge tumor volumes in fetal gut-immunized ($m = 0.9$ cm^3) and whole embryo-immunized animals ($m = 0.9$ cm^3) were less ($p < 0.05$) than in fetal kidney-immunized ($m = 2.5$ cm^3) or adult-colon-immunized animals ($m = 1.8$ cm^3). Low-dose NG-W1 challenge tumor volumes were less ($p < 0.01$) in multiparous females ($m = 0.3$ cm^3) than in either untreated ($m = 1.2$ cm^3) or age-matched virgins ($m = 1.4$ cm^3). In vitro tumor markers in this model may serve an important function in vivo as TRA's. (11 refs.)

77-4592 **Detection of Selectively Incorporated H-2 Antigens in Disrupted, But Not Intact Friend Virus**

Particles (Meeting Abstract). (Eng.) Bubbers, J. E. (Dept. Genetics, Albert Einstein Coll. Medicine, Bronx, NY 10461) Chen, S.; Lilly, F. *Proc Am Assoc Cancer Res* 18: 43; 1977. (no refs.)

77-4593 **A Cautionary Note Regarding Ia and H-2 Typing of Murine Lymphoid Tumors.** (Eng.) Wettstein, P. J. (Genetics Curriculum, Dept. Bacteriology and Immunology, Univ. North Carolina, Chapel Hill, NC 27514) Krammer, P.; Nowinski, R. C.; Davis, C. S.; Frelinger, J. A.; Shreffler, D. C. *Immunogenetics* 3(5): 507-516; 1976.

The expression of I region-associated (Ia) antigens on AKR thymomas was characterized. Tumor lines were characterized as Ia-positive by positive reaction with anti-Ia (k) antisera in complement-dependent cytotoxic tests, by absorption of anti-Ia (k) activity for normal lymphocytes by tumor cell preparations, and by absorption and elution of specific anti-Ia (k) antibodies from tumor cell preparations. The spontaneous AKR (H-2(k):Ia. 1,2,3,7) thymomas were studied. Of 74 tested, 23 thymoma lines showed significant lysis with A.TH and anti-A.TL antiserum as a 1:20 or greater dilution and were tentatively classified Ia-positive. Nine tumors (seven Ia-positive and two Ia-negative) were studied further. Unexpected nonspecific reactions with (B10.M x A.TL)F_1 anti-A.TH and A.TL anti-A.TH antisera were observed with six of the tumors; five of these six had originally tested as positive with A.TH and anti-A.TL antiserum. Further examination showed that these nonspecific reactions were the consequence of contaminant antibodies against murine leukemia virus that coexisted in the Ia antisera. Contaminant host lymphocytes, comprising as little as 1% of the total tumor cell population, were found to be responsible for the positive absorption and elution results of the tumor cell preparation. That the tested AKR thymomas do express Ia antigen still must be resolved. (21 refs.)

77-4594 **HLA Frequencies in Cancer: A Second Study.** (Eng.) Terasaki, P. I. (Dept. Surgery, Univ. California, Los Angeles, CA 90024) Perdue, S. T.; Mickey, M. R. *Prog Cancer Res Ther* 3: 321-328; 1977.

The frequencies of 25 HLA antigens were studied in over 6,000 cancer patients and in over 5,200 controls. The study indicated a high incidence of HLA-A2 in acute lymphocytic leukemia and, in prostatic cancer, a low HLA-A1 and HLA-B8 along with elevated HLA-A28 and HLA-BW22. (9 refs.)

77-4595 **HLA-A9 and Survival in Acute Lymphocytic Leukemia and Myelocytic Leukemia.** (Eng.) Cohen, E. (Dept. Breast Surgery, Roswell Park Memorial Inst., Buffalo, NY 14263) Singal, D. P.; Khurana, U.; Gregory, S. G.; Cox, C.; Sinks, L.; Henderson, E.; Fitzpatrick, J. E.; Higby, D. *Prog Clin Biol Res* 16: 65-70; 1977.

There is a positive relationship between survival in acute lymphocytic leukemia patients and the HLA-A9 histocompatibility antigen, but not with acute myelogenous leukemia patients and the antigen. (8 refs.)

77-4596 **Normal Adult Murine Cells Express Oncofetal Antigens in Tissue Culture (Meeting Abstract).** (Eng.) Parker, G. A. (NCI, NIH, Bethesda, MD 20014) *Proc Am Assoc Cancer Res* 18: 205; 1977. (no refs.)

77-4597 **Alpha-Fetoprotein in Rats Treated with Antithymocytic Serum.** (Eng.) Boss, J. H. (Dept. Pathology, Hebrew Univ.-Hadassah Medical Sch., Post Office Box 24035, Jerusalem, Israel) Okon, E.; Rosemann, E. *Biomedicine [Express]* 27(4): 150-154; 1977.

The presence of α-fetoprotein (AFP) was investigated in the sera of (1) untreated female Sabra rats, (2) rats fed a diet containing the hepatocarcinogen 3′-methyl-4-dimethylaminoazobenzene (3-MeDAB: 0.06% in the diet), (3) rats fed the 3-MeDAB diet and administered an ip injection of antithymocytic serum (ATS: 0.5 ml), and (4) rats fed a normal diet and injected with ATS. AFP was not detected in rats of Groups 1 or 2, but it was found in 8/10 and 8/11 rats from Groups 3 and 4, respectively. Groups 3 and 4 rats developed glomerulonephritis. It is suggested that the elevation of serum AFP in the nephritic rats is related to compensatory hyperplasia of the liver parenchymal cells, stimulated by hypoproteinemia resulting from urinary protein loss. (20 refs.)

77-4598 **CEA-Like Substance in Normal Colon Washings (Meeting Abstract).** (Eng.) Egan, M. L. (Univ. Alabama in Birmingham, Birmingham, AL 35294) Pritchard, D. G.; Shively, J. E.; Go, V. L. *Proc Am Assoc Cancer Res* 18: 40; 1977. (no refs.)

77-4599 **Isoantigenic Expression of Forssman Glycolipid in Human Gastric and Colonic Mucosa: Its Possible Identity with "A-like Antigen" in Human Cancer.** (Eng.) Hakomori, S. (Div. Biochemical Oncology, Fred Hutchinson Cancer Res. Center, Seattle, WA 98104); Wang, S.

M.; Young, W. W. *Proc Natl Acad Sci USA* 74(7): 3023-3027; 1977.

The Forssman glycolipid and its precursor globoside were examined in 21 samples of surgically removed gastrointestinal mucosa and tumors. Hemolysis inhibition and liposome lysis assays of the ceramide tetrasaccharide and pentasaccharide fractions of the 21 samples indicated that 16 patients lacked Forssman activity (F-) and 5 showed positive activity (F+). The F- population included blood groups A, B, and O, but none of the F+ group belonged to blood group A. All tumors derived from F- mucosa contained significant levels of Forssman reactivity, but none of the tumors originating in F+ mucosa contained Forssman glycolipid. Globoside, the immediate precursor of Forssman antigen, was distributed equally among F+ and F- mucosa and tumors. The expression of the Forssman antigen in gastrointestinal mucosa appears, therefore, similar to that of an isoantigen and could represent a human tumor-associated antigen. In view of the well-known strong cross reactivity of Forssman antigen with blood group A determinants, it is suggested that the appearance of Forssman antigen in human tumors could be related to the previously described "A-like antigen" (or neo-A antigen) of human tumors. (32 refs.)

77-4600 **Leukocyte Adherence Inhibition by Soluble Tumor Antigens in Breast Cancer Patients.** (Eng.) Fujisawa, T. (Dept. General and Oncologic Surgery, City of Hope Natl. Medical Center, Duarte, CA); Waldman, S. R.; Yonemoto, R. H. *Cancer* 39(2): 506-513; 1977.

Specific cell-mediated immunity to selected extracts of breast cancer was demonstrated in breast cancer patients with a modified and refined Leukocyte Adherence Inhibition Assay (LAI). No significant difference was noted in LAI at different clinical stages of the disease nor at various stages following mastectomy. Specific responses were also demonstrated in colon cancer patients and melanoma patients to the appropriate extract. (26 refs.)

77-4601 **An Overview: Antitumor Immunity in Breast Cancer Assayed by Tube Leukocyte Adherence Inhibition.** (Eng.) Flores, M. (Montreal General Hosp. Res. Inst., Div. Clinical Immunology and Allergy, Montreal, Quebec, Canada); Marti, J. H.; Grosser, N.; MacFarlane, J. K.; Thompson, D. M. *Cancer* 39(2): 494-505; 1977.

Results of a lymphocyte adherence inhibition assay done on a large number of breast cancer patients (Stages I, II, III, and IV) suggest that lack of leukocyte reactivity and the presence of serum blocking indicate an excess of tumor antigen from a large tumor mass that is blocking tumor immunity. (39 refs.)

77-4602 **Malignancy in Relatives of "Non-responders" to Rh Antigen (Letter to Editor).** (Eng.) Cook, I. A. (North of Scotland Blood Transfusion Service, Raigmore Hosp., Inverness, Scotland) Shepherd, S. *Br Med J* 2(6089): 771; 1977.

Detailed medical and family histories of Rh negative men, 21 who could be immunized to the Rh antigen (responders) and 25 who could not (non-responders) revealed 13 confirmed malignancies among 267 relatives in the non-responder group. In the responder group, there were 6 confirmed cases among 297 relatives. Further studies should include at least 100 individuals in each group. (3 refs.)

77-4603 **Evidence for Deranged Cellular Immunoregulation in Malignancy (Meeting Abstract).** (Eng.) Hammer, C. (McGill Univ., Cancer Res. Unit., McIntyre Medical Sciences Building, 3655 Drummond St., Montreal, Quebec H3G 1Y6, Canada) Lewis, M. G. *Eur Surg Res* 9(4): 289-290; 1977. (4 refs.)

77-4604 **Endometrial Carcinoma Associated with Azathioprine and Cortisone Therapy. A Case Report.** (Eng.) Hodgkinson, D. J. (Mayo Clinic, 200 First St. S. W., Rochester, MN 55901) Williams, T. J. *Gynecol Oncol* 5(3): 308-312; 1977.

The case history of a 43-yr-old woman who developed endometrial carcinoma following a 16 mo treatment with prednisone and a 14-mo treatment with azathioprine is presented. Amenorrhea without estrogenic stimulation was present for 20 yr and was attributed to ovarian failure and high levels of gonadotropin. It is suggested that the drug-induced immunosuppression was important in the development of malignancy. (17 refs.)

77-4605 **Macrophage-Lymphocyte Rosettes of Lymph Node Aspirates in Patients with Skin Cancer: Suggestive Evidence for Physical Interaction Between Immune Lymphocytes and Macrophages.** (Eng.) Friedman, M. (Dept. Radiation Medicine, Roswell Park Memorial Inst., New York State Dept. Health, 666 Elm St., Buffalo, NY 14263) Han, T. *IRCS Med Sci: Cancer* 5(5): 223; 1977.

Macrophage-lymphocyte rosettes were observed in smears of materials aspirated from cancer-draining hyperplastic lymph nodes in two patients with skin cancer. The patients were a 71-yr-old man with ulcerated basal cell carcinoma involving the right orbit and a 60-yr-old woman with a huge mass involving the left tibial circumference. Smears were made on glass slides, stained according to the Wright-Giemsa technique, and examined by light microscopy. The rosettes consisted of macrophages attached by many small hyperchromatic lymphocytes. The mechanism of macrophage-lymphocyte formation in lymph node aspirates of skin cancer patients is not known. The rosette formation suggests a physical interaction between immune lymphocytes and macrophages. (10 refs.)

77-4606 **Recognition and Destruction of Tumor Target Cells by Activated Macrophages (Meeting Abstract).** (Eng.) Fidler, I. J. (NCI--Frederick Cancer Res. Center, Frederick, MD 21701) *Proc Am Assoc Cancer Res* 18: 3; 1977. (no refs.)

77-4607 **Insulin Inhibition of Antibody-dependent Cytoxicity and Insulin Receptors in Macrophages.** (Eng.) Bar, R. S. (Diabetes Branch, Natl. Inst. Arthritis, Metabolism and Digestive Diseases, NIH, Bethesda, MD 20014); Kahn, C. R.; Koren, H. S. *Nature* 265(5595): 632-635; 1977.

The existence of insulin receptors in macrophage and insulin inhibition of antibody-dependent cell-mediated cytotoxicity (ADCC) were investigated in cultured mouse tumor macrophages (P388D), macrophage-containing cell populations from normal mouse spleens, and human mononuclear cells. ^{125}I-insulin binding to P338D cells, mouse spleen cells, and human mononuclear cells. ^{125}I-insulin binding to P338D cells, mouse spleen cells, and human mononuclear cells demonstrated properties that characterize classical insulin receptors. The receptors on all three cell types showed similar inhibition of insulin binding by insulin analogs, with the receptor potency of the insulin analog being proportional to its biological activity. Several physicochemical properties of the insulin receptors in these cell populations were similar to more classical insulin receptors. The results of equilibrium analyses and kinetic studies of insulin binding indicated site-site interactions among insulin receptors of the negatively cooperative type. Insulin inhibited ADCC in both the tumor macrophages and the mixed cell population from mouse spleens. Insulin inhibition was most pronounced at low effector-to-target cell ratios. In the spleen cells, insulin maximally inhibited ADCC by 30%, but in the more homogenous P388D cells, insulin inhibited ADCC by > 70%. These findings indicate that macrophages from normal mouse spleens and cultured tumor macrophages possess insulin receptors indistinguishable from those of the circulating human monocyte and that physiological concentrations of insulin alter a specific immunological function, ADCC, in both spleen and tumor cells. (26 refs.)

77-4608 **Studies on the Mechanism of Interferon Action: Characterization of Polysome-associated Cellular RNA's Modified by Interferon.** (Eng.) Riley, F. L. (Lab. Viral Diseases, Natl. Inst. Allergy and Infectious Diseases, NIH, Bethesda, MD 20014); Levy, H. B. *Virology* 76(1): 459-463; 1977.

Data show that the polysome-associated RNA species that are altered in interferon-treated cells are poly(A)-containing messenger RNA's (mRNA's), RNA's without a poly(A)-rich region, and transfer RNA's (tRNA's). Interferon mRNA's may be slightly larger than normal, as they migrate more slowly than control cell mRNA's in polyacrylamide gels in both aqueous and nonaqueous media. Interferon tRNA's, however, move more slowly than controls in aqueous medium only, suggesting that the difference in motility in tRNA's is associated with factors other than size. (17 refs.)

77-4609 **The Use of Specific Antibodies to Study the Cell Surface of Transformed and Untransformed Syrian Hamster Cells (Meeting Abstract).** (Eng.) Clarke, S. M. (Univ. Colorado Medical Sch., Denver, CO 80262) Fink, L. M. *Proc Am Assoc Cancer Res* 18: 18; 1977. (no refs.)

77-4610 **Inhibition of Antibody-Dependent Cellular Cytotoxicity by Protein A from *Staphylococcus Aureus*.** (Eng.) Rosenblatt, J. (Immunobiology Group, Dept. Microbiology and Immunology, Univ. California at Los Angeles Sch. Medicine, Los Angeles, CA 90024); Zeltzer, P. M.; Portaro, J.; Seeger, R. C. *J Immunol* 118(3): 981-985; 1977.

Antibody-dependent cellular cytotoxicity (ADCC) was inhibited by and dependent upon relative concentrations of protein A and anti-target cell antiserum. Because protein A also inhibited rosette formation between sheep RBC and lymphoid cells with Fc receptors, it was concluded that protein A inhibits ADCC by preventing binding of antibody-coated target cells to Fc receptors on cytotoxic effector cells. (29 refs.)

77-4611 **Appearance of a Variant of MOPC 104E Which Does Not React with Dextran B-1355s.** (Eng.) Folds, J. D. (Dept. Bacteriology and Immunology, Sch. Medicine, Univ. North Carolina, Chapel Hill, NC 27514). *Immunol Commun* 6(4): 385-394; 1977.

A variant of the mouse plastocytoma MOPC 104E tumor, which produces an IgM (λ) melanoma protein that does not bind dextran B-1355s, is reported. Lack of binding specificity was determined by (1) the absence of precipitin lines in Ouchterlony analysis, (2) the fact that dextran B-1355s does not absorb the IgM spike found in variant serum but does absorb the IgM spike found in normal MOPC 104E serum, and (3) lack of absorption of the variant protein to an immunoabsorbant dextran B1355s-Sepharose preparation. The variant does, however, react with anti-IgM antisera. The variant and normal IgM's have similar electrophoretic mobilities in microzone electrophoresis, and the variant IgM elutes from Sephadex B-200 columns in the void volume. Both IgM's react with anti-λ light-chain antiserum. The variant tumor arose spontaneously in the laboratory and appears to be stable. One possible explanation for this tumor is a point mutation in the V region of viral DNA. (12 refs.)

77-4612 **Receptors for IgM-coated Erythrocytes on Chronic Lymphatic Leukemia Cells.** (Eng.) Pichler, W. J. (Inst. Immunology, Univ. Vienna, A-1090 Vienna, Austria); Knapp, W. *J Immunol* 118(3): 1010-1015; 1977.

Results of inhibition studies using lymphocytes from 18 patients with chronic lymphocytic leukemia (CLL) show that binding of bovine RBC coated with IgM antibody does not occur via a somewhat altered IgG-Fc receptor, but reacts with different membrane structures. In CLL patients, the IgM receptors were demonstrable before overnight cultivation and were found on cells with B-cell characteristics. (27 refs.)

77-4613 **Solubilization and Partial Characterization of Cell Membrane Fc Receptors.** (Eng.) Anderson, C. L. (Natl. Jewish Hosp. and Res. Center, Denver, CO 80206); Grey, H. M. *J Immunol* 118(3): 819-825; 1977.

Evidence indicated that an inhibitory activity measured with the mastocytoma-aggregated immunoglobulin G inhibition assay was soluble plasma membrane Fc receptor. A method for obtaining Fc receptors in soluble form, an assay for quantitating their presence, and some physicochemical features of the solubilized receptors are discussed. (33 refs.)

77-4614 **The Locomotory Behaviour of the Multinucleate Giant Cells of Foreign Body Reactions.** (Eng.) Papadimitriou, J. M. (Dept. Pathology, Univ. W. Australia, Perth Medical Centre, Shenton Park, Australia 6008); Kingston, K. J. *J Pathol* 121(1): 27-36; 1977.

The locomotory behavior of the murine multinucleate giant cells produced in foreign body reactions is described. Foreign body giant cells were produced by sc implantation of glass coverslips or cellophane into the dorsum of C57 black or BALB/c mice. Implants were removed after 2 wk. Cinemicrographic observations of the multinucleate giant cells showed that they are a highly pleomorphic population displaying constantly changing, complex, and varying shapes. Locomotion on a glass substratum by these polykaryocytes varied, depending mainly on size. Generally, the translocational movement of the macrophages (3-10 μm/min was faster than that of the polykaryocytes. The translocation speed was 0.3-1.0 μm/min for polykaryocytes with 2-4 nuclei and 0.04 μm/min for polykaryocytes with >15 nuclei. This behavior would tend to maintain these cells near their formation site. The direction of translocation of the small syncytia correlated with that of the single leading lamellipodium. Slightly larger cells (5-15 nuclei) showed loss of polarity, with multiple lamellipodia, but the syncytia with >15 nuclei possessed a single, large, circumferential lamellipodium whose movement led to little displacement. The latter also displayed reduced contact inhibition. The cellular movement of the polykaryocytes depended on continuing glycolysis, physiological concentrations of calcium, and on intact microtubules and microfilaments. (91 refs.)

See also:
* (Rev.): 77-4233, 77-4238, 77-4239, 77-4240, 77-4244, 77-4253.
* (Chem.): 77-4313, 77-4357, 77-4425.
* (Phys.): 77-4473, 77-4480, 77-4485.
* (Viral.): 77-4496, 77-4509, 77-4521, 77-4534, 77-4536, 77-4546.
* (Path.): 77-4629, 77-4650, 77-4673.

PATHOGENESIS

77-4615 **The Influence of Untreated Internal Mammary Metastases upon the Course of Mammary Cancer.** (Eng.) Donegan, W. L. (Div. Surgery, Medical Coll. Wisconsin, Box 145, 8700 W. Wisconsin, Milwaukee, WI 53226) *Cancer* 39(2): 533-538; 1977.

The records of all cases of breast cancer seen at one hospital between 1949 and 1965 were reviewed. Among the 2,621 cases, 113 had been treated with standard radical mastectomy and they also had an ipsilateral internal mammary (IM) node biopsy. The long-term follow-up (av 13.6 yr) of these cases is reported. Twenty-five cases were found to have IM metastases: the highest frequencies occurred in the presence of axillary metastases, medial primaries, and clinically advanced cancers. For example, 22/25 cases also had axillary spread. IM metastases were associated with poor survival--only 5/20 patients with positive biopsies (excluding 5 who were treated) survived 5 yr, and 1 for 10 yr. Corresponding figures for the 85 patients with negative biopsies were 53% and 32%. The survival of 5 patients with IM metastases who were treated with postoperative irradiation or castration was not superior to that of the 20 untreated patients. Neither in the presence nor absence of axillary involvement did IM metastases have a significant influence upon treatment failure. It is concluded that IM metastases usually reflect generalized tumor spread and that local therapy directed at these nodes has a negligible influence upon cure. (13 refs.)

77-4616 **A Comparative Study of Some Pathologic Features of Mammary Carcinoma in Tokyo, Japan and New York, USA.** (Eng.) Rosen, P. P. (Dept. Pathology, Memorial Hosp., 1275 York Ave., New York, NY 10021); Ashikari, R.; Thaler, H.; Ishikawa, S.; Hirota, T.; Abe, O.; Yamamoto, H.; Beattie, E. J.; Urban, J. A.; Mike, V. *Cancer* 39(2): 429-434; 1977.

The histopathologic characteristics of breast carcinomas treated at the National Cancer Center Hospital (NCH) in Tokyo in 1973-1974 and at Memorial Sloan-Kettering Cancer Center (MH) in New York in 1974 are presented. The former group consisted of 216 and the latter of 555 carcinomas. The age range of the patients at both hospitals was 24-82 yr, but the av age was 50.2 yr at NCH and 58 yr at MH. There were four major findings: (1) a high frequency of colloid and of medullary carcinoma with lymphoid stroma and a lesser frequency of lobular carcinoma in the Japanese patients; (2) more intense lymphoid infiltrate in and around primary tumors in Japanese women; (3) higher frequency of rounded or circumscribed tumors in Japanese women; and (4) a more frequent occurrence of intralymphatic tumor emboli within the breast in American women. Over the past 20 yr, the percentage of patients with no axillary metastases has improved from 43% to 56% at MH and from 51% to 63% at NCH. This improvement was also manifested by an almost identical decrease in the frequency with which metastases were demonstrated at Level III (22%-13% at MH, 17%-9% at NCH). (21 refs.)

77-4617 **Prospective Study of Non-infiltrating Carcinoma of the Breast.** (Eng.) Ashikari, R. (Dept. Surgery, Memorial Hosp., 1275 York Ave., New York, NY 10021) Huvos, A. G.; Snyder, R. E. *Cancer* 39(2): 435-439; 1977.

Data concerning diagnosis and pathological findings of preinvasive or noninfiltrating carcinoma (CA) of the breast (lobular in situ and intraductal CA) are given. A total of 175 patients (31-76 yr, av 52), 88 with lobular CA, 71 with intraductal CA, and 16 with both types, were followed for 11 yr. Of those with the lobular form, 46 presented with a breast mass, 26 had thickening, and 2 had nipple discharge. The intraductal CA group presented with a breast mass in 30 cases, thickening in 14, and nipple discharge in 11. Preoperative mammograms of 102 patients were positive or suspicious in 57% of those with lobular CA and 74% with intraductal CA. The usual findings were an abnormal density or a localized cluster of calcifications. Noninfiltrating CA was diagnosed on frozen sections in 35% of cases (18% lobular and 55% intraductal); the remainder were diagnosed on permanent paraffin sections. The histology of the intraductal lesions was variable, with single or multiple layers of malignant cells occurring within the ducts. Often the entire lumen was filled with proliferating cells, with central necrosis presenting the comedo pattern. The lobular lesions were characterized by proliferating cells filling and distending the lobules and occasionally extending into the terminal ductules. The cellular arrangement was loose or compact, lacking an orderly pattern. On pathological exam of mastectomy specimens, 36% of all patients (42% lobular and 30% intraductal) had multicentric focal lesions in different quadrants from the primary lesion. (8 refs.)

77-4618 **Association of Breast Cancer with Myeloproliferative Disorders.** (Eng.) Cornfield, D. B. (Jeanes Hosp., 7600 Central Ave., Philadelphia, PA 19111); Binder, R. A.; Rath, C. E. *South Med J* 70(7): 780-783; 1977.

The occurrence of myeloproliferative disorders in three breast cancer patients is described. The first patient had a left radical mastectomy at age 36 followed by irradiation to the left chest wall, axilla, and ovaries. She required a right radical mastectomy and postoperative irradiation at age 57 for infiltrating ductal carcinoma with metastases to five axillary lymph nodes. Two years later, solitary metastatic masses were excised from her right upper arm and forearm; 5 yr later, at age 62, she presented with pancytopenia. Autopsy revealed progressive leukemic infiltration of the spleen, bone marrow, liver, and mediastinal lymph nodes. Breast cancer was found only in the mediastinal lymph nodes. The second woman (age 65 yr) presented with chronic myelogenous leukemia 3 yr after simple mastectomy and po diethylstilbestrol therapy for breast cancer. Two years later, osteoblastic lesions were discovered in her thoracic and lumbar vertebrae. Postmortem examination revealed breast carcinoma metastatic to the axillae, plurae, lung, liver, kidney, peritoneum, and bone. The third case is of a 54-yr-old woman who presented with polycythemia vera. Nine years later she had a right radical mastectomy for a 3-cm infiltrating adenocarcinoma. The patient died at age 70 with metastases to the liver, spleen, pericardium, pleurae, and bone marrow and extramedullary hematopoieses in the liver, spleen, and kidneys. Bone marrow biopsy showed metastatic carcinoma, myelofibrosis, and panmyelosis. The occurrence of breast cancer and myeloproliferative disorders in an individual may be more than a chance occurrence. These disorders may be related via some common inducing mechanism such as infection or chemical carcinogenesis. (16 refs.)

77-4619 **Retrograde Lymphatic Spread and Ischemia of the Forearm and Hand--Rare Complications of Carcinoma of the Breast.** (Eng.) Metcalf, J. S. (Dept. Pathology, Medical Univ. South Carolina, 80 Barre St., Charleston, SC 29401) O'Brien, P. H.; Kreutner, A. *Cancer* 40(1): 371-375; 1977.

A 52-yr-old woman who had had a left simple mastectomy for breast cancer 3 yr previously underwent mid-forearm amputation for ischemia of the forearm and hand with necrosis. Histology indicated extensive lymphatic involvement by tumor. This spread is believed to be the result of retrograde lymphatic extension. (5 refs.)

77-4620 **Ultrastructure of Human Endometrial Epithelium in Monolayer Culture with and Without Steroid Hormones.** (Eng.) Liszczak, T. M. (Dept. Surgery, Massachusetts General Hosp., Boston, MA 02114); Richardson, G. S.; MacLaughlin, D. T.; Kornblith, P. L. *In Vitro* 13(6): 344-356; 1977.

Monolayer cultures consisting of glandular epithelial cells free of connective tissue cells of stromal or other origin were established from explants of human endometrium. The epithelial cells were separated from stromal cells by cloning cylinders. Their ultrastructural properties were compared to those of fresh endometrium, and characteristics of the glandular epithelium cells were noted in both. Colonies of epithelioid cells persisted for 40-50 days in 4/8 cultures. The overall appearance of the epithelioid cells was consistent with that of the in vivo tissue. Similar features included junctional complexes consisting of macula adherens, zonula adherens, and zonula occludens; perinuclear microfilaments in close association with glycogen deposits, and microvilli surrounded by a glycocalyx. Other common features were prominent nucleoli, well-developed Golgi apparatus, rough endoplasmic reticulum, and membrane-bound electron-dense bodies in the cytoplasm. Aliquots of the epithelioid cells were grown in hormone-free medium, in the presence of 10^{-6} M estradiol and/or progesterone for 1 wk. The cellular morphology was not affected by the presence or absence of hormone. (26 refs.)

77-4621 **On the Histogenesis of Mixed Uterine Tumors.** (Ger.) Schmitt, K. (Richard-Wagner-Str. 45, 6750 Kaiserslautern 1, W. Germany) Schafer, A. *Oesterr Z Onkol* 3(5/6): 122-126; 1976.

A study of five cases of mixed uterine tumors indicated that these tumors were not of dispersed embryogenic isles of Mullerian duct origin; rather, the multipotency of proliferating cells was noted later in connection with metaplasia in older patients. (36 refs.)

77-4622 **The Induction of Precancerous Changes in the Uterine Epithelium of the Rat: The Role of Spermatozoa.** (Eng.) Stein-Werblowsky, R. (Bikur Cholim Hosp., Jerusalem, Israel) *Gynecol Oncol* 5(3): 251-261; 1977.

Pathological changes were noted in the cervical epithelium of white Wistar rats after currettage of the uterine horn followed by artificial insemination and natural mating. An extrapolation of these results to humans may indicate that sperm penetration at a time when there is a break in mucous membrane continuity could be an initial event in the development of uterine cancer. (10 refs.)

77-4623 **Ovarian Tumors and Related Lesions in Aged Chimpanzees.** (Eng.) Graham, C. E. (Yerkes Regional Primate Res. Center, Emory Univ., Atlanta, GA) McClure, H. M. *Vet Pathol* 14(4): 380-386; 1977.

A 48-yr-old female chimpanzee developed large bilateral ovarian fibrothecomas and a 39-yr-old chimpanzee had two small fibrothecomas in one ovary and a well-differentiated Sertoli-Leydig cell tumor in the other. These two cases support the hypothesis that thecal hypertrophy in chimpanzees can be associated with hyperestrogenism and endometrial hyperplasia. The histology of these tumors is also discussed. (11 refs.)

77-4624 **Lipid Cell Tumor of the Ovary: An Ultrastructural Study.** (Eng.) Ishida, T. (Dept. Obstetrics and Gynecology, Univ. Minnesota Medical Sch., Minneapolis, MN 55455) Okagaki, T.; Tagatz, G. E.; Jacobson, M. E.; Doe, R. P. *Cancer* 40(1): 234-243; 1977.

An ultrastructural evaluation of a lipid cell tumor from a woman with secondary amenorrhea, hirsutism, and elevated 17-ketosteroid excretion indicated that the tumor was derived from the ovarian stroma. She had taken oral contraceptives for 4 yr, and her symptoms began 1 yr after discontinuation of their use. (46 refs.)

77-4625 **The Incidence and Significance of Polynuclear Follicles.** (Eng.) Sherrer, C. W. (Dept. Obstetrics and Gynecology, Johns Hopkins Medical Institutions, Baltimore, MD 21205) Gerson, B.; Woodruff, J. D. *Am J Obstet Gynecol* 128(1): 6-12; 1977.

When ovarian tissue from 165 patients was examined microscopically, polynuclear follicles were found for all age groups through the fifth decade. The incidence decreased from 57% in patients <20 yr old to 0% in those >40. No association with contraceptives was noted. The relationship of polynuclear follicles to the development of teratomas is discussed. (20 refs.)

77-4626 **Choriocarcinoma in Mother and Child (Meeting Abstract).** (Dut.) van Lent, M. (Leiden, Netherlands) Nieuwenhuyzen Kruseman, A. C. *Ned Tijdschr Geneeskd* 120(41): 1766-1767; 1976. (no refs.)

77-4627 **Experimental Rat Choriocarcinoma--An Electron Microscopic Study.** (Eng.) Kakudo, K. (Dept. Pathology, Osaka Univ. Medical Sch., Osaka-shi, Kita-ku, Joan- cho 33, Japan 530). *Acta Pathol Jpn* 27(1): 41-50; 1977.

Three primary choriocarcinomas induced in pregnant Wistar rats were compared ultrastructurally with specimens of normal rat placenta at the mid- and late-gestational stages. Common features were desmosomelike attachments at the cell surface of the tumors and numerous free ribosomes, polysomes, and rough-surfaced endoplasmic reticulum in the cytoplasm. The many ultrastructural differences noted are also discussed. (15 refs.)

77-4628 **Congenital Total Hemihypertrophy and Carcinoma of Undescended Testicle: A Case Report.** (Eng.) Parra, G. (Dept. Surgery, Div. Urology, Long Island Jewish-Hillside Medical Center, New Hyde Park, NY) Seery, W.; Buchbinder, M.; Cole, A. T. *J Urol* 118(2): 343-344; 1977.

A 54-yr-old man with multiple congenital anomalies (hemihypertrophy, cryptorchidism, medullary sponge kidney, cafe au lait spots) developed a germinal cell tumor in the undescended testis. A high incidence of malignancy is associated with this form of teratogenesis. (6 refs.)

77-4629 **Humoral Antibodies Against Spermatopoietic Cells Associated with Mediastinal Germinoma.** (Eng.) Buerki, H. (Inst. Pathology, Univ. Bern, Freiburgstrasse 30, CH-3010 Bern, Switzerland) Locher, G. W.; Graepel, P.; Ruchti, C.; Brun del Re, G.; Hess, M. W. *J Pathol* 121(3): 183-186; 1977.

The case history of a 21-yr-old man with mediastinal germinoma is described. The neoplasm exhibited a morphology similar to that of a testicular seminoma and was heavily infiltrated by lymphocytes and plasma cells. Germinal centers were seen in the lymph follicles. Humoral antibodies specific for spermatopoietic tissue were present in the serum; however, after surgical removal of the germinoma, antibody titers declined over a period of 2 yr to undetectable levels. The finding that the serum contained specific antibodies against homologous spermatopoietic cells is consistent with the suggestion that mediastinal germinomas are derived from ectopic germ cells. (8 refs.)

77-4630 **Theories of Pathogenesis: Mutation and Cancer.** (Eng.) Strong, L. C. (Graduate Sch. Biomedical Sciences, Univ. Texas Health Science Center, Houston, TX 77030) *Prog Cancer Res Ther* 3: 401-415; 1977.

Several observations have led to the conclusion that carcinogenesis is a two-step mutational process in which either step might occur spontaneously or might be induced by another carcinogen, ie radiation. These observations include the long latent period for most cancers, independent of dosage; saturation kinetics of the dose-response curve for radiation carcinogenesis; an increased incidence of tumors in subjects receiving multiple exposures (compared to a single exposure of the same total dose). According to the two-mutation model, the first step may be inherited or acquired, but the second would always be acquired. Two disorders in which there is a tissue-specific hereditary predisposition to tumor and a frequent exposure to radiation are hereditary retinoblastoma (RB) and the nevoid basal cell carcinoma syndrome (NBCCS). Several tables of data on radiation-treated survivors of childhood cancer and the radiogenic malignancies that ensued are included. RB patients generally received a much higher total radiation dose, and radiogenic sarcomas were more common

ong survivors of bilateral RB (67%) than among survivors
other childhood malignancy (35.7%). The latent period for
diogenic malignancy in bilateral RB patients was shorter,
th a unique peak incidence in the fifth and sixth posttreat-
ent years. Concerning the NBCCS, the group in which
diation effects are most pronounced is marked by develop-
ent of medulloblastoma and is treated with radiation to the
anium and spinal axis. A recent case occurring in a young
l is reported. Studies of individuals who inherit the first
utation may reveal important characteristics of the sequen-
l steps in carcinogenesis. (76 refs.)

7-4631 **Delayed Mutation Model: Carotid Body Tumors and Retinoblastoma.** (Eng.) Herrmann, J.
Dept. Pediatrics, Univ. Wisconsin, Madison, WI 53706)
rog Cancer Res Ther 3: 417-438; 1977.

he delayed mutation was applied to data on carotid body
imors (CBT) and retinoblastoma (RB). A previous study
owed that the pattern of pedigrees with multiple (unaffect-
d) carriers was consistent for each condition, but that signifi-
ant differences existed between the pattern of different con-
itions. The differences concerned telomutation rate, sex of
arriers and affected individuals, the occurrence of delayed
utation in germinal and somatic cells, and the proportion
f delayed and complete mutation at a particular locus. These
spects are illustrated. They indicate that several mechanisms
ay be involved in delayed mutation and that the model has
roader implications than is assumed. Pedigrees of reported
amilial instances of CBT and RB in man are summarized,
nd the corresponding numerical data are tabulated. The RB
ene may be a cause of true mosaic pleiotropy, which can be
vident in two ways: different members of the same family
ay be affected by different tumors (including RB) and a
atient with RB may subsequently develop another malig-
ancy, all caused by the RB gene. According to an interpreta-
ion of RB genetic data, they can be explained by a single
autosomal dominant mutation that can be complete or
delayed and can occur in germinal and somatic cells. Devel-
opment or nondevelopment of tumor foci, tumor growth, and
unilateral and bilateral involvement of RB in mutant in-
dividuals represent variable expressivity related to patho-
genesis of cancer. Although not fully understood, this ex-
pressivity is also observed in many other dominant human
neoplasia syndromes, such as Gardner's syndrome, neurofi-
bromatosis, and intestinal polyposis. (84 refs.)

77-4632 **Congenital Teratoma of the Orbit.** (Eng.) Barishak, Y. R. (Eye Pathology Lab., Tel Hashomer
Hosp., Tel Aviv, Israel) Mashiah, M. *J Pediatr Ophthalmol*
14(4): 217-220; 1977.

The case history of a newborn girl with a congenital teratoma of the orbit is presented. Exenteration was performed because of the suspicion of malignant tumor. Histologic analysis revealed three germinal layers of tumor tissue showing an advanced degree of differentiation. (5 refs.)

77-4633 **Neoplasm of Mixed Mesenchymal and Neuroepithelial Origin of the Optic Nerve.** (Eng.) Shuangshoti, S. (Dept. Pathology, Faculty Medicine, Chulalongkorn Univ., Bangkok 5, Thailand) Panyathanya, R. *Br J Ophthalmol* 61(6): 390-393; 1977.

A case is presented of an 18-yr-old man with a mixed meningioma and astrocytoma of the right eye. This case indicates that these two neoplasms can arise in the optic nerve (having a sheath analogous to the leptomeninges) and form a mixed neoplasm. (14 refs.)

77-4634 **Classification of Experimental Brain Tumors.** (Ger.) Schreiber, D. (Pathologisches Institut der Martin-Luther Universitat Halle-Wittenberg, DDR-402 Halle, Leninallee 14, E. Germany) Janisch, W.; Rath, F. *Exp Pathol (Jena)* 13(1): 3-10; 1977.

Problems associated with the classification of experimental brain tumors were investigated. Tumors were induced by ethylnitrosourea or methylnitrosourea in newborn or adult rats or by transplacental application of these agents. Serial sections were performed through the cerebrum of 57 rats to detect early tumor stages and their localization in the brain. In other rats, the brain and spinal cord were investigated. A total of 174 small tumors, most <2 mm in diameter, were found. The early tumor stages never involved the ependyma of the ventricular walls or the central canal of the spinal cord. The tumors exhibited strong acid phosphatase activity, but the ependymal cells were negative for the enzyme. No true rosettes, cilia, or basal granules were seen in the tumors; no perivascular zones free of nuclei were found. The experimental ependymomas reported in the literature have been diagnosed on the basis of rowlike arrangements of tumor cells. Similar structures were present in the large oligodendrogliomas and glioblastomas, suggesting that the classification of experimental brain tumors as ependymomas is not always justified. Because of the significance of experimental results for human neurooncology, the criteria of histogenetic classification should be applied rigorously. (17 refs.)

77-4635 **Association of Von Recklinghausen's Disease and Neuroblastoma in a Young Child.** (Ita.) Gemme, G. (Clinica Pediatrica "G. Gaslini" dell'Universita di Genova, Genoa, Italy); Guarino, M.; Ruffa, G.; Bonioli, E.; Paita, G. *Minerva Pediatr* 29(19): 1255-1260; 1977.

A 31-mo-old boy, who exhibited the classical symptoms of von Recklinghausen's disease, also underwent surgery for the removal of a left suprarenal ganglioneuroblastoma. It was hypothesized that the two diseases have a common genetic origin, starting from the embryonal cells of the neural crest. (21 refs.)

77-4636 **Olfactory Neuroblastoma: An Ultrastructural Study.** (Eng.) Taxy, J. B. (Dept. Army, Medical Res. Inst. Infectious Diseases, Pathology Div., Fort Detrick, Frederick, MD 21701) Hidvegi, D. F. *Cancer* 39(1): 131-138; 1977.

Two olfactory neuroblastomas, one arising in the nasal cavity of an 18-yr-old girl and the other in the left maxilly sinus of a 25-yr-old woman, were studied by light and electron microscopy. The second patient had undergone radiotherapy at age 16 for a malignant fibrous histiocytoma in the same location. Light microscopy revealed a typical, well-differentiated olfactory neuroblastoma in the first case, but only a poorly differentiated small cell neoplasm in the second. The latter case required the ultrastructural demonstration of numerous cystoplasmic processes to establish the diagnosis. No catecholamines were detected biochemically in the recurrent tumor, suggesting that olfactory neuroblastomas may not be as metabolically active as sympathetic neuroblastomas. However, these tumors are morphologically similar by light and electron microscopy. (40 refs.)

77-4637 **Neoplasms Associated with Formes Frustes of Beckwith-Wiedemann Syndrome (Meeting Abstract).** (Eng.) Sotelo-Avila, C. (Univ. Tennessee Center for Health Sciences, Memphis, TN) Rosenberg, H. S. *Am J Pathol* 86(2): 3a; 1977. (1 ref.)

77-4638 **A Prospective Study of Parotid Metastases from Head and Neck Cancer.** (Eng.) Storm, F. K. (54-140 CHS, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA 90024); Eilber, F. R.; Sparks, F. C.; Morton, D. L. *Am J Surg;* 1977.

Eighty-eight patients with cutaneous head and neck cancers were studied to determine which cancers tend to metastasize to the parotid lymph nodes. The findings suggest that patients with potentially metastatic primary cancer of the eyelid, frontal, temporal, posterior cheek, and anterior ear regions are at risk for parotid node metastasis. (7 refs.)

77-4639 **Ultrastructural Changes and Viral Morphogenesis During the Growth of the Mouse Preputial Gland Tumor ESR 586.** (Eng.) Prutkin, L. (Dept. Cel Biology, New York Univ. Schs. Medicine, New York, NY 10016) Rossman, T. G.; Wheatley, V. R. *Cancer Res* 37(2) 551-556; 1977.

Morphological changes and viral morphogenesis during th growth of the mouse preputial gland tumor ESR 586 wer studied by electron microscopy. The acinar cells of the normal preputial gland have an extensive agranular endoplasmic reticulum and Golgi apparatus and large lipid droplets. N viral particles are present. During tumor growth, the numerous lipid droplets never attain the size of those found in th normal gland. There is a decrease in the Golgi apparatus an agranular endoplasmic reticulum and an increase in th rough endoplasmic reticulum that could reflect a change i composition of the tumor secretory product from the norma gland. There is, in fact, a decrease in triglycerides and a increase in sterol esters and waxes as the tumor ages. In addition, intracisternal A-type particles are observed buddin from thickened endoplasmic reticulum membranes. Thickening of these membranes occurs early in A-particle formation One side of the membrane is first thickened while the opposing membrane appears morphologically unaffected. Thickening of the affected membrane is initially confined to the oute (cytoplasmic) face of the membrane. In the older tumor, bot opposing membranes of the reticulum are thickened, and the can assume an elongated whorled pattern. (25 refs.)

77-4640 **Histochemical and Ultrastructural Studies o Chemodectoma-like Tumors in the Cod (*Gadus Morrhua* L.).** (Eng.) Lange, E. (Dept. Pathology, Norsk Hydro's Inst. Cancer Res., Norwegian Radium Hosp., Oslo, Norway) Johannessen, J. V. *Lab Invest* 37(1): 96-104; 1977.

Thirty-six tumors in the cephalic region of 21 cod (*Gadu morrhua* L.) caught in the inner part of the Oslo fjord were examined histochemically and ultrastructurally. Tumors were frequently located bilaterally in the pseudobranches, and they could be described as either adenomas or adenocarcinomas of epithelial origin. Light microscopy revealed a organoid tissue pattern with argyrophil fibers surrounding nests of light and dark cells, possible lipofuscin content, and inconclusive argentaffin and chromaffin reactions. Despite infiltrating tumor growth indicating malignant potential, the peripheral contours of the tumors were usually rounded. Numerous membrane-limited granules were observed by electron microscopy. The ultrastructural appearance of the tumors suggested their similarity to the extra-adrenal paraganglion system and other endocrine tumors in humans. The pseudobranches, from which the tumors appear to be derived, may function as chemoreceptors that could be affected by pollution or the oxygen content of the water. (29 refs.)

77-4641 **Pheochromocytoma with Angiomatous Features. A Case Report and Ultrastructural Study.** (Eng.) Shin, W. Y. (Dept. Pathology, Long Island Jewish-

Hillside Medical Center, New Hyde Park, NY 11040) Groman, G. S.; Berkman, J. I. *Cancer* 40(1): 275-283; 1977.

An ultrastructural study of a pheochromocytoma from a 43-yr-old woman indicated that the catecholamine granules probably arise from the region of the endoplasmic reticulum at the inner (trans) aspect of the Golgi apparatus that gives rise to coated vesicles and other lysosomes and from other regions of the endoplasmic reticulum. The tumor had a angiomatous histologic pattern. (10 refs.)

77-4642 **A Case of Parathyroid Carcinoma Concurred with Hyperplasia: An Electron Microscopic Study.** (Eng.) Murayama, T. (Urology Service, Sanraku Hosp., Chiyoda-ku, Tokyo 101, Japan) Kawabe, K.; Tagami, M. *J Urol* 118(1/part 1): 126-127; 1977.

The case history of a 46-yr-old man with concurrent parathyroid carcinoma and chief cell hyperplasia, each in different glands, is discussed. Electron microscopy revealed interdigitating plasma membranes and many cytoplasmic secretory granules in the neoplastic cells. (4 refs.)

77-4643 **Pigmented Hyperplasia of Epidermis Following Feeding of L-Dopa to Elderly Rats.** (Eng.) Maat, B. (Radiobiological Inst. TNO, 151 Lange Kleiweg, Rijswijk ZH, The Netherlands). *J Natl Cancer Inst* 58(5): 1433-1436; 1977.

L-Dopa was administered to aged, male BN rats at a dose of 200 mg/kg/day, po, until death. Of the treated animals, 11% showed local pigmented epidermal hyperplasia, compared with only 0.5% of controls. However, the number of expected malignant melanomas was not increased by L-dopa treatment. (20 refs.)

77-4644 **Electron Histochemical Study of Phosphorylase System in Choroidal Melanoma.** (Eng.) Amemiya, T. (Dept. Ophthalmology, Faculty Medicine Kyoto Univ., Sakyo-ku, Kyoto-shi, Japan 606). *Acta Histochem (Jena)* 58(1): 56-62; 1977.

An electron histochemical study of four human choroidal melanomas failed to identify the cell types of choroidal melanoma by the morphologic appearance of polyglucose particles synthesized by phosphorylase and branching glycosyltransferase. These results indicate no difference in glycolysis among spindle B cells, epithelioid cells, and melanophages of choroidal melanomas. (9 refs.)

77-4645 **Ultrastructure of Spontaneously Differentiated Human Malignant Melanocytes Cultured from Primary Tumors.** (Eng.) Aubert, C. (Unite 119 de l'Institut National de la Sante et de la Recherche Medicale, 27 Bd Lei Roure 13009 Marseille, France) Chirieceanu, E.; Foa, C.; Delain, E. *J Natl Cancer Inst* 58(1): 29-35; 1977.

An ultrastructural study of early subcultures and established lines of human malignant melanocytes derived from primary tumors showed that the melanocytes passed through a dedifferentiation phase during which they took on a fibroblastlike appearance. This was followed by a phase of spontaneous redifferentiation. The fibroblast-like cells were characterized by the presence of network-type organelles in their cytoplasm and the redifferentiated melanocytes were characterized by the presence of melanosomes. (18 refs.)

77-4646 **The Ultrastructure of Lymphadenosis Benigna Cutis (Pseudolymphoma Cutis).** (Eng.) Schmoeckel, C. (Dermatolofiaxhw Klinik und Poliklinik der Universitat Munchen, Frauenlobstrasse 9, D-8000 Munich 2) Burg, G.; Wolf, H. H.; Braun-Falco, O. *Arch Dermatol Res* 258(2): 161-167; 1977.

Electron and light microscopy investigations of biopsies from six patients with lymphadenosis benigna cutis showed that the tumor consists of lymphocytes and large macrophagocytic cells. Signs of degenerative changes are in accordance with the tendency of these lesions to regress spontaneously. (13 refs.)

77-4647 **Tumors in Xeroderma Pigmentosum (Meeting Abstract).** (Dut.) van Doormaal, T. A. (Breda, Netherlands) Harmsen, A. E.; Pompe, C. A. *Ned Tijdschr Geneeskd* 120(44): 1913-1914; 1977.

A 19-yr-old girl with xeroderma pigmentosum developed the following malignant tumors during the course of her disease: 4 basal carcinomas, 1 basal cell epithelioma, 6 squamous cell carcinomas, 1 mixed basal cell carcinoma-spindle cell carcinoma, 3 fibrosarcomas, 1 liposarcoma, 2 hemangiosarcomas, 10 malignant melanomas, 1 amelanotic melanoma, and 1 keratoacanthoma. In addition, 22 benign or precancerous tumors were identified. (2 refs.)

77-4648 **Nevus Cell Aggregates Associated with Lymph Nodes: Estimated Frequency and Clinical Significance.** (Eng.) Ridolfi, R. L. (Dept. Pathology, Memorial Sloan-Kettering Cancer Center, 1275 York

Ave., New York, NY 10021) Rosen, P. P.; Thaler, H. *Cancer* 39(1): 164-171; 1977.

Slides of lymph nodes from 909 mastectomy specimens and from 100 patients with malignant melanoma were examined for the frequency of nevus cell aggregates (NCA). The NCA were present in 3/17,504 axillary lymph nodes from the breast cancer patients and in 3/2,607 lymph nodes from the melanoma patients. In the latter group, the axillary nodes were involved in two cases and a cervical node in one. The NCA could be distinguished from metastatic tumors by their localization within the fibrous capsule and/or associated trabeculae of the lymph nodes. The possibility that they are a potential source of malignant melanoma in patients without a demonstrable cutaneous or mucosal primary is discussed. (18 refs.)

77-4649 **Carcinoma of the Cardia and Thoracic Oesophagus Coexisting with and Following Sliding Hiatal Hernia and Peptic Stricture.** (Eng.) Moghissi, K. (Humberside Cardiothoracic Surgical Centre, Castle Hill Hosp., Cottingham, N. Humberside, England). *Thorax* 32(3): 342-345; 1977.

The relationship between hiatal hernia or peptic stricture and carcinoma was studied in a series of 207 patients with carcinoma of the cardia and thoracic esophagus. In one group of 10 cases of adenocarcinoma coexisting with hiatal hernia (9.8% of the those with carcinoma of the cardia), sufficient evidence was not available to determine whether hiatal hernia predisposes to carcinoma or whether the relationship is merely coincidental. In another group of 5 patients (2.4%), a long-standing hiatal hernia with chronic esophagitis and benign peptic stricture preceded the development of carcinoma by 3-15 yr. Thus, malignant changes may occur in cases of chronic peptic stricture, especially when reconstructive surgery is not performed, as in two patients in this group. (8 refs.)

77-4650 **Alarming Cures!** (Fre.) Monod, E. (Centre Hospitalier d'Avignon, Avignon, France) *Rev Fr Gastroenterol* (123): 29-32; 1976.

A prior spontaneous amelioration of digestive and allergic disorders occurred in some patients who eventually developed cancer. Of 235 cancer patients who completed a standardized questionnaire, 29 disclosed that they had experienced an unexplained amelioration of chronic digestive and allergic (particularly migraine) disorders some months or years prior to the onset of clinical tumor signs. The case histories of five patients [carcinomas of the sigmoid, pancreas, stomach (2), and rectum] who experienced this remission are reviewed. It is hypothesized that the phenomenon represents a form of immunosuppression. (4 refs.)

77-4651 **Nephrotic Syndrome Associated with Gastric Cancer.** (Eng.) Catane, R. (Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263); Kaufman, J. H.; Douglass, H. O.; Kim, U.; Mittelman, A. *J Surg Oncol* 9(1): 207-211; 1977.

A 47-yr-old man whose nephrotic syndrome was controlled by prednisone and cyclophosphamide for approx 1 yr was found to have gastric cancer. There was no recurrence of the nephrotic syndrome symptoms following removal of the tumor and discontinuation of the steroid therapy. (16 refs.)

77-4652 **Studies of the Growth and Infiltration of Experimental Tumor of the Pancreas in Rabbits.** (Eng.) Nakase, A. (First Div. Surgery, Kyoto Univ. Medical Sch., Sakyo-ku, Kyoto, Japan); Koizumi, T.; Fujita, N.; Ono, H.; Honjo, I.; Matsumoto, Y. *Am J Surg* 133(5): 590-592; 1977.

Vx2 carcinoma was transplanted into the pancreatic duct of rabbits, and its growth pattern was assessed. Four experimental groups of 10 animals each were used: (A) the pancreatic duct was punctured near its opening in the duodenum and 0.4-0.6 ml carcinoma supernatant was injected into the tail of the pancreas; the duct was ligated at the injection site; (B) same as Group A, but the pancreatic duct was not ligated; (C) pancreatic duct was ligated in the midportion of the pancreas, and 0.2-0.25 ml supernatant was injected into the duct near the duodenal opening; the duct was ligated at the injection site; (D) the duct was ligated in the midportion, and 0.2-0.25 ml of supernatant was injected on the tail side of the ligation with the needle tip directed toward the tail. The presence of ductal obstruction assisted the transplantation and growth of cancer cells in the pancreas. Tumors induced in the head grew by extension to the body and tail, where they also produced interspersed, nodular tumor masses. Those induced in the body and tail grew by direct expansion toward the head, but they did not produce the interspersed nodular tumors in the head. These results indicate that cancer of the head, associated with stenosis or obstruction of the duct, resulted in ductal dissemination and extensive lymphatic infiltration in the body and tail, a wider invasion than was recognizable at the gross cancer border. This extension was noncontinuous and interspersed, so that radical curative surgery would indicate total pancreatectomy. (4 refs.)

77-4653 **Malignant Metaplasia Risk in Organs with Atrophic and Hypertrophic-Hyperplastic Changes.** (Cze.) Knezevic, S. (Zagreb, Smiciklasova 9, Yugoslavia); Knezevic, S. *Cas Lek Cesk* 116(15): 449451; 1977.

Increased α-fetoprotein (AFP) levels were found in 32/174 atients with chronic hepatitis, 26/68 patients with acute epatitis, and 10/13 patients with primary liver cancer. The fect of AFP on regenerative foci with hypertrophic-yperplastic cellular changes may lead to malignant metalasia. (5 refs.)

7-4654 **Hepatocellular Carcinoma and Chronic Persistent Hepatitis.** (Eng.) Shikata, T. (Dept. Patholoy, Nihon Univ. Sch. Medicine, Ohyaguchi-Kamimachi, tabashiku, Tokyo, 173, Japan); Yamazaki, S.; Uzawa, T. *Acta Pathol Jpn* 27(3): 297-304; 1977.

A study was made of 220 hepatocellular carcinoma (HC) ases from 9,000 consecutive autopsies performed during 949-1973 to clarify the nature of the cirrhosis and fibrosis ssociated with this neoplasm. Of the 220 cases, cirrhosis was ound in 181, liver fibrosis in 17. The morphologic type of irrhosis that was followed most frequently by HC was posthepatitis cirrhosis. Ten HC cases with fibrosis, 6 with early irrhosis, and 3 without either were chosen to determine the presence of hepatitis B surface antigen (HBsAg) in the tissue. HBsAg was detected in 4/10, 4/6, and 0/3 of the paraffin ections, respectively. These results suggest that there is an ntimate causal relationship between hepatitis B virus and HC. In addition, detection of HBsAg in 40% of the HC cases with fibrosis led to the conclusion that since some cases of ibrosis are caused by chronic viral hepatitis, HC may develop not only on posthepatitis cirrhosis, but also on chronic peristent hepatitis. (14 refs.)

77-4655 **Observations by Scanning Electron Microscopy of Normal and Pathological Human Gall Bladder Epithelium.** (Eng.) Myllarniemi, H. (Second Dept. Surgery, Univ. Helsinki, Helsinki, Finland) Nickels, J. I. *Acta Pathol Microbiol SCand [A]* 85(1): 42-48; 1977.

Two normal gallbladders and 11 gallbladders from patients with cholesterolosis (6) or chronic cholecystitis (5) were studied by light and scanning microscopy. Adenomyomatosis was present in two cases of chronic cholecystitis, and mucosal hyperplasia was present in one case of cholesterolosis and two cases of chronic cholecystitis. In the bladders of patients with cholesterolosis the mucosal folds were clearly dilated, but the individual epithelial cells had retained their normal hexagonal structure. In the gallbladder of one patient with cholesterolosis, gobletlike cells were seen in the epithelium. The greatest changes were found in the specimens from patients with severe chronic cholecystitis. The mucosal folds were clearly flattened, the cell boundaries were indistinct, and small polypoid structures were present on the surface of the epithelium. No special changes were seen in gallbladders from the patients with adenomyomatosis or mucosal hyperplasia. (15 refs.)

77-4656 **Cholecystectomy and Carcinoma of the Colon. An Experimental Study.** (Eng.) Werner, B. (Dept. General Surgery, Univ. Hosps. Hamburg, Martinistrasse 52, D-2000 Hamburg 20, W. Germany) de Heer, K.; Mitschke, H. *Z Krebsforsch* 88(3): 223-230; 1977.

A total of 70% of female NMRI mice that had undergone cholecystectomy developed carcinoma of the colon after receiving 1,2-dimethylhydrazine (15 mg/kg/wk x 10, sc), compared to only 16% of animals treated similarly but without cholecystectomy. Removal of the gallbladder may render the colon more sensitive to exogenous carcinogens. (22 refs.)

77-4657 **Carcinoma of the Ileum in Regional Ileitis.** (Eng.) Gude, H. E. (Iowa Falls, IA). *J Iowa Med Soc* 67(8): 324-325; 1977.

A case is reported of a 62-yr-old woman with a 22-yr history of regional ileitis and subsequent adenocarcinoma of the ileum. This case provides evidence that development of carcinoma is related to long-term Crohn's disease. (2 refs.)

77-4658 **Bowen's Carcinoma in Vulvovaginal Crohn's Disease (Regional Enterocolitis): Report of First Case.** (Eng.) Prezyna, A. P. (Dept. Tissue Pathology, Buffalo General Hosp., 100 High St., Buffalo, NY 14203) Kalyanaraman, U. *Am J Obstet Gynecol* 128(8): 914-916; 1977.

The first known case of Crohn's disease of the vulvovaginal area with development of Bowen's carcinoma occurred in a 36-yr-old woman. The potential for areas involved with Crohn's disease to undergo malignant change is emphasized. (2 refs.)

77-4659 **Mucoepidermoid Carcinoma in an "Anal Fistula" with Associated Adenocarcinoma in a Villous Adenoma of the Descending Colon: Report of a Case.** (Eng.) Fogler, R. (625 Rockaway Parkway, Brooklyn, NY 11236); Lanter, B.; Stern, G.; Weiner, E. *Dis Colon Rectum* 20(5): 428-435; 1977.

The case history is presented of a 57-yr-old man with mucoepidermoid carcinoma of the anal canal extending to the perineum with involvement of the villous tract, and adenocarcinoma and mucoepidermoid carcinoma arising in villous adenoma of the splenic flexure of the colon. The histology of these tumors is presented. This case illustrates the controversy over tumor cell origin of these neoplasms. (9 refs.)

77-4660 **Colonic Adenocarcinoma: A Delayed Complication of Ureterosigmoidostomy.** (Eng.) Parsons, C. D. (Dept. Urology, Indiana Univ. Medical Center, Indianapolis, IN) Thomas, M. H.; Garrett, R. A. *J Urol* 118(1/part 1): 31-34; 1977.

Case reports are presented of two men who developed colonic adenocarcinoma at the site of a previous ureterosigmoidostomy. The carcinomas developed 26 and 33 yr, respectively, after the surgery. It is suggested that a pseudopolyploid mucosal fold at the anastomotic site undergoes adenomatous degeneration to carcinoma as a result of chronic irritation. (23 refs.)

77-4661 **Development of Sigmoid Carcinoma after Ureterosigmoidostomy.** (Ger.) Ecke, M. (Urologische Klinik der Medizinischen Akademie Magdeburg, Magdeburg, E. Germany) Muller, G. W. *Z Urol Nephrol* 70(6): 391-397; 1977.

The case of a 52-yr-old woman with sigmoid carcinoma is presented. A ureterosigmoidostomy (UST) had been performed in 1959. The patient was symptom-free for 15 yr, when she rapidly lost 20 kg, and had bloody stools. Laparotomy confirmed a sigmoid tumor in the vicinity of the ureterosigmoidal anastomosis. Resection of the sigmoid colon, end-to-end anastomosis, and another UST were done. In 1976 the patient was still well with no sign of recurrence. Data from a literature review (1929-1976) are tabulated for 27 men and 12 women with sigmoid tumors. The av age of the patients with malignancies was 61 yr, those with benign tumors 34 yr. The latency period ranged from 1 to 46 yr, with a median of 18.5 yr. Of 100,000 UST's performed, 13,300 were for sigmoid carcinoma. In the US, this carcinoma occurs in 2.3/100,000 people 40-44 yr old; in Germany the figure is 4/100,000 for the same age group. Urine retention and bloody stools are signs of possible sigmoid carcinoma. Diagnosis is by histological examination, urography, sigmoidoscopy, and x-ray contrast enemas. (35 refs.)

77-4662 **Renal Cell Carcinoma Presenting as Vaginal Bleeding.** (Eng.) Knight, E. L. (Dept. Urology, West Virginia Univ. Medical Center, Morgantown, WV 26506) Kandzari, S. J.; Milam, D. F. *Urology* 10(3): 249-250; 1977.

The case history of a 79-yr-old woman with renal cell carcinoma is presented. Vaginal bleeding was the result of a metastasis. The dissemination mechanism of tumor emboli is discussed. (10 refs.)

77-4663 **Needle Tract Seeding of Renal Cell Carcinoma.** (Eng.) Bush, W. H. (Dept. Radiology, Mason Clinic and Virginia Mason Medical Center, 1100 Ninth Ave Seattle, WA 98111); Burnett, L. L.; Gibbons, R. P. *Am Roentgenol* 129(4): 725-727; 1977.

The case history of a 56-yr-old man with renal cell carcinom which metastasized along the line of a needle biopsy is pr sented. It is suggested that this first report of such an occur rence need not deter the use of renal cyst aspiration, especia ly since the patient's survival was not adversely affected. (2 refs.)

77-4664 **Early Detection but Delayed Appearance of Bladder Tumor.** (Eng.) Marshall, V. F. (Dept Surgery, James Bucahan Brady Foundation, New York, NY Seybolt, J. F. *J Urol* 118(1/part 2): 175-176; 1977.

The case is presented of a 57-yr-old man who died of transi tional cell carcinoma of the bladder and renal pelvis 20 y after the detection of malignant cells by urinary cytolog (Papanicolaou method). This is the longest such interval o record. (13 refs.)

77-4665 **Significance of Proliferative Lesions of Bladde (Letter to Editor).** (Eng.) Coggi, G. (Dept. His topathology, Univ. Milan, 20090 Milan, Italy) Arpa, P. *Lan cet* 2(8030): 189; 1977.

Autopsy studies indicated that proliferative lesions of th bladder were found in 97% of the cadavers that were free c malignant disease. This high incidence suggests that thes lesions are not preneoplastic and that their presence in malig nant tissues has no etiological significance. (1 ref.)

77-4666 **Human Bladder Carcinoma: Characterizatio of Two New Tumor Cell Lines and Search fo Tumor Viruses.** (Eng.) Rasheed, S. (Dept. Pathology, Univ Southern California Sch. Medicine, Los Angeles, CA 90033 Gardner, M. B.; Rongey, R. W.; Nelson-Rees, W. A.; Arn stein, P. *J Natl Cancer Inst* 58(4): 881-890; 1977.

Two new cell lines (HT-1197 and HT-1376) derived fron transitional cell carcinomas of the bladder were character ized. Cells of both cultures exhibited fine structural microvill and tonofibrils indicative of their epithelial origin. In addi tion, desmosomes were present in HT-1197. The marke chromosomes of HT-1197 and HT-1376 distinguished th two lines from each other and from the other known tumo cell lines studied by chromosome-banding. Both culture grew in soft agar, induced fibrinolytic activity, and wer tumorigenic in NIH nude mice and immunodeficient ham sters. No C-type virus was detected in these cell lines, in 2 bladder and kidney carcinomas examined by culture or elec ron microscopy, or in rejected renal allografts or WBC from mmunosuppressed renal transplant patients. (37 refs.)

7-4667 **Mesotheliomas of the Tunica Vaginalis Propria and Peritoneum in Fischer Rats.** (Eng.) Gould, D. H. (Western Regional Res. Lab., Agricultural Res. Service, U.S. Dept. Agriculture, Berkeley, CA) *Vet Pathol* 14(4): 372-379; 1977.

Nine mesotheliomas were found in a group of 384 male Fischer rats maintained on a heated soy oil diet, processed cottonseed meal diet, 2.5% or 5% neohesperidin dihydrochalcone, or a control basal diet. No relation was found between tumorigenesis and any of the test materials, although 4/9 cases had mesotheliomatous involvement of the peritoneal as well as genital mesothelium. (35 refs.)

77-4668 **Rhabdomyosarcoma of Lung Arising in Congenital Cystic Adenomatoid Malformation.** (Eng.) Ueda, K. (Dept. Pathology, Children's Hosp. Medical Center, Elland and Bethesda Aves., Cincinnati, OH 45229) Gruppo, R.; Unger, F.; Martin, L.; Bove, K. *Cancer* 40(1): 383-388; 1977.

The case history of an 18-mo-old girl with an asymptomatic congenital adenomatoid malformation of the lung harboring a rhabdomyosarcoma is presented. The sarcoma was discovered by chance 14 mo later, when the malformation was removed. Her tumor-free interval now exceeds 3 yr. (26 refs.)

77-4669 **Pulmonary Blastoma: An Ultrastructural Study with a Brief Review of Literature and a Discussion of Pathogenesis.** (Eng.) Fung, C. H. (Mercy Hosp. and Medical Center, Stevenson Expressway at King Drive, Chicago, IL 60616) Lo, J. W.; Yonan, T. N.; Milloy, F. J.; Hakami, M. M.; Changus, G. W. *Cancer* 39(1): 153-163; 1977.

The case of a 19-yr-old woman with a metastatic pulmonary blastoma is reported. The light and electron microscopic features of the tumor resembled those of the fetal lung before the fourth gestational month. Although the ultrastructural findings did not disprove any particular theory of histogenesis, they did not support the concept that these tumors arise from a pluripotential pulmonary blastema. Of the 38 other pulmonary blastomas reported in the literature, 30 were in males and 8 in females; the age range was 2 mo to 77 yr, with an av age of 39 yr. Metastases were present in approx one-half of the cases. (60 refs.)

77-4670 **Cervical Angiofollicular Lymph Node Hyperplasia.** (Eng.) Weintraub, M. I. (Medcoa Building, 990 Grand Canyon Parkway, Hoffman Estates, IL 60194) Shibata, C. *Laryngoscope* 87(9/Part 1): 1543-1547; 1977.

The case of a 3 1/2-yr-old boy with cervical angiofollicular lymph node hyperplasia is presented. Although the exact origin of the hyperplasia is unknown, it has a favorable outcome and should not be mistaken for a lymphoma. (10 refs.)

77-4671 **Light and Electron Microscopic Investigation of the Pathogenesis of Kaposi's Sarcoma.** (Ger.) Heine, H. (Anatomisches Institut der Universitat, Koellikerstrasse 6, D-8700 Wurzburg, W. Germany) Schaeg, G.; Nasemann, T. *Arch Dermatol Res* 258(2): 175-184; 1977.

Skin biopsies of a 69-yr-old man with Kaposi's sarcoma (KS) were investigated by light and electron microscopy. The areas affected were both lower thighs, the tops of the feet, and the lower arms. The results show that in KS, the normal metabolism between the endothelial cells, matrix, and fibrocytes is disturbed. The extracellular matrix is changed, and, via a feedback mechanism, the CNS and the endocrine system are affected. The results of this feedback process are conversion of fibrocytes into tumor cells and disruption of the endothelial cells. Synthesis of the matrix in the vicinity of the tumor seems to proceed from myocyte-type cells, as suggested by their strongly developed Golgi apparatus and the vesicular formation of the cell membrane. The activity of the cell surface seems to be due to pino- and exocytotic processes. Various theories of the histogenesis of KS are discussed. (24 refs.)

77-4672 **Thrombocythaemia and Multiple Myeloma. A Report on Two Cases.** (Eng.) Selroos, O. (Fourth Dept. Medicine, Helsinki Univ. Central Hosp., Helsinki, Finland); van Assendelft, A. *Acta Med Scand* 201(3): 243-247; 1977.

Two unusual cases of essential thrombocythemia combined with multiple myeloma are reported. In both patients, a diagnosis of multiple myeloma was indicated by an increase in plasma cells in the bone marrow, multiple osteolytic lesions in the skeleton, and a monoclonal increase in kappa-type serum immunoglobulins. In addition, both had hemorrhagic diathesis, thrombotic complications, and a platelet count > 1 million/mm^2. Symptoms and signs related to the thrombocythemia were observed only 6 mo (case 1) and 14 mo (case 2) prior to detection of the myeloma. Thus, it is impossible to determine which disease preceded the other. The first patient responded well to melphalan. In case 2, thrombocythemia was controlled with busulphan, but the patient died of a thromboembolic complication before treatment of the myeloma was started. The possibility of a common agent initiating both malignant processes at the same time should be considered. (14 refs.)

77-4673 **Erythema Elevatum Diutinum and IgA Myeloma: An Interesting Association.** (Eng.) Archimandritis, A. J. (Dept. Pathological Physiology, Section Internal Medicine, Medical Sch., Univ. Athens, Athens 609, Greece) Fertakis, A.; Alegakis, G.; Bartsokas, S.; Melissinos, K. *Br Med J* 2(6087): 613-614; 1977.

The case history of a 53-yr-old woman with IgA myeloma is presented. The myeloma was diagnosed 9 yr after the appearance of erythema elevatum diutinum and 5 yr after the discovery of paraproteinemia. (5 refs.)

77-4674 **Hb G Norfolk Associated with Malignant Myelosclerosis (Letter to Editor).** (Eng.) Higgs, D. R. (King's Coll. Hosp. Medical Sch., Univ. London, Dept. Haematology, Denmark Hill, London SE5 8RX, England) Frost, B.; Sharp, J. C. L. *Lancet* 2(8036): 513; 1977.

An abnormal Hb, HbG Norfolk, was detected by electrophoresis in an 81-yr-old man with malignant myelosclerosis. This finding is most commonly found in erythremic myelosis. The other three cases of HbG Norfolk in the literature are noted. (6 refs.)

77-4675 **Chronic Myelocytic Leukemia: Clonal Origin in a Stem Cell Common to the Granulocyte, Erythrocyte, Platelet and Monocyte/Macrophage.** (Eng.) Fialkow, P. J. (Medical Service, Veterans Admin. Hosp., 4435 Beacon Ave. S., Seattle, WA 98108); Jacobson, R. J.; Papayannopoulou, T. *Am J Med* 63(1): 125-130; 1977.

The X-linked enzyme glucose-6-phosphate dehydrogenase (G-6-PD) was used as a marker to investigate the etiology and pathogenesis of chronic myelocytic leukemia (CML). G-6-PD isoenzyme types in the granulocytes were determined in eight black women (15-86 yr old) with CML. The patients were heterozygous at the X-linked G-6-PD locus for the common gene, *Gd-B*, and a variant, *Gd-A*, so that on direct analysis of skin and in cultures of skin fibroblasts, both B and A enzymes were found. In contrast, single-enzyme phenotypes were observed in CML granulocytes. Four patients had type B enzyme and four had type A. These findings provide strong evidence that CML has a clonal origin. Single-enzyme phenotypes were also found in RBC, platelets, and cultured blood macrophages, indicating that these cells have a common stem cell that is the site of abnormality in CML. Cultures of marrow fibroblasts were studied from only one patient, and there was no evidence for involvement of these cells. The clonal origin of CML virtually excludes cell recruitment as the sole pathogenetic mechanism. The fact that, at the time of diagnosis, the leukemia cells are all clonally derived indicates that the initiating oncogenic event is rare and/or that a series of steps occurs before a clone evolves into clinically evident CML. (35 refs.)

77-4676 **Ultrastructural Cytochemical Analysis of Blastic Transformation of Chronic Myelocytic Leukemia.** (Eng.) Palakavongs, P. (Dept. Medicine, North Shore Univ. Hosp., Manhasset, NY 11030) Teichberg, S.; Vinciguerra, V.; Degnan, T. J.; Sinlaratana, P. *Blood* 49(4): 535-547; 1977.

Cytochemical changes in the distribution of myeloperoxidase, which occur during the blast phase of chronic myelocytic leukemia (CML), suggest that immature leukemic cells alter their patterns of secretory granule production. This may reflect the emergence of an abnormal clone of cells during the blastic transformation of CML. (42 refs.)

77-4677 **Ph^1-positive Childhood Leukemias: Spectrum of Lymphoid-Myeloid Expressions.** (Eng.) Forman, E. N. (Div. Pediatric Hematology-Oncology, Rhode Island Hosp., 593 Eddy St., Providence, RI 02902) Padre-Mendoza, T.; Smith, P. S.; Barker, B. E.; Farnes, P. *Blood* 49(4): 549-558; 1977.

Chromosome preparations and cell culture studies of two children, ages 4 and 9 yr, with Ph^1-positive leukemia produced evidence that supports the assumption of mixed lymphoid-myeloid properties of blast cells in chronic myelocytic leukemia in children. Some pediatric leukemias may present with complex stem cell relationships. (25 refs.)

77-4678 **Physicochemical Properties of DNP Systems of Leukemic Cells with Different Numbers of Chromosomes.** (Eng.) Svirnovskii, A. I. (Lab. Pathophysiology Leukemia, Belorussian Scientific-Res. Inst. Hematology and Blood Transfusion, Minsk, USSR); Nikolaichik, V. V.; Levin, V. I. *Bull Exp Biol Med* 83(1): 97-100; 1977.

Investigation of the thermomechanical and disaggregation properties of supramolecular DNP systems isolated from leukemic cells from AKR and C57BL mice indicated a stronger than normal bond between their components. This property was independent of the subpopulation to which the cells belonged and of their chromosome number. (14 refs.)

77-4679 **Effects of Mutant Steel Alleles on Leukemogenesis and Life-span in the Mouse.** (Eng.) Murphy, E. D. (Jackson Lab., Bar Harbor, ME 04609) *J Natl Cancer Inst* 58(1): 107-110; 1977.

Mutant alleles at the steel locus (chromosome 10) produce the pleiotropic effects of congenital anemia, sterility, and lack of hair pigmentation. (WC/Re x C57BL/6)F_1, SI/SId mice lived only half as long as heterozygotes and homozygous normal controls, differing only at the steel locus. Lymphocytic leukemia developed spontaneously in 37% of mice of the SI/SId genotype at an av age of 370 ± 25 days and in 5% of heterozygotes and homozygous normal controls at 965 ± 41 days. Severe ulcerative dermatis occurred in 55% of SI/SId mice at an av age of 441 ± 21 days and in 20% of heterozygotes and homozygous normal controls at 722 ± 50 days. With mutant steel alleles, one can study the role of chronic anemia in life shortening and the action of genes in spontaneous leukemogenesis. (24 refs.)

77-4680 **Familial Islet-cell Adenomatosis.** (Eng.) Tragl, K. H. (First Medical Clinic, Univ. Vienna, A-1090 Wien, Lazarettgasse 14, Austria) Mayr, W. R. *Lancet* 2(8035): 426-428; 1977.

A familial occurrence of multiple adenoma of pancreatic beta cells is reported. Since diabetes mellitus occurred in different family members, the possibility of a genetic disorder as the basis for both the adenoma and diabetes is suggested. HLA typing did not indicate a connection between the HLA complex and the autosomal dominant gene probably responsible for this disorder. (23 refs.)

77-4681 **Immunochemical Markers and Hereditary Cancer Risk (Meeting Abstract).** (Eng.) Guirgis, H. A. (Dept. Preventive Medicine/Public Health, Creighton Univ., Omaha, NB 68178) Lynch, H. T.; Lemon, H. M.; Caha, L.; Maloney, K.; Carmody, L.; Lynch, J.; Swartz, M.; Lynch, P. *Proc Am Assoc Cancer Res* 18: 192; 1977. (no refs.)

77-4682 **Age Dependence of Chromosomal Aberrations.** (Ger.) Vormittag, W. (II. Medizinische Universitatsklinik, Garnisongasse 13, A-1090, Vienna, Austria) *Acta Med Austriaca* 4(1): 1-5; 1977.

Review of the literature and studies of peripheral blood lymphocytes from women confirm that premature centromere division, the incidence of dicentric chromosomes, and the frequency of single chromosome breaks are higher in old women than in young ones. (29 refs.)

77-4683 **Some Features of Expression of Genetic Information in Cells with Aneuploid Set of Chromosomes.** (Rus.) Annenkov, G. A. (Inst. Medical Genetics, Acad. Medical Sciences USSR, Moscow, USSR) Tamarkina, A. D. *Vestn Akad Med Nauk SSSR* (3): 32-36; 1977.

Activities of acid and alkaline phosphatases, lactate dehydrogenase (LDH), malate dehydrogenase and glutamic-oxaloacetic transaminase (GOT) were assessed spectrophotometrically in fibroblast cultures from patients with trisomies 7, 9, 13, 14, and 21 (Down's syndrome) and in patients with X-chromosome abnormalities [XO, XXX, XXY (Klinefelter's syndrome), and XXXXY]. MDH activity was significantly elevated in patients with trisomies 13 and 14 (172% and 313%, respectively) and in patients with Klinefelter's syndrome (204%). Alkaline phosphatase activity was significantly inhibited in patients with trisomies 13, 14, 7, and 9 (32%, 5.5%, 11.3%, and 17.7%, respectively) and in patients with Klinefelter's syndrome (27.5%). Acid phosphatase activity was decreased in patients with trisomy 14 (36%), trisomy 9 (46.3%), and trisomy 7 (76%). Activities of all enzymes but alkaline phosphatase were decreased in patients with Down's syndrome. Since the acid phosphatase locus is mapped on chromosome 11, MDH locus on chromosome 7, GOT locus on 10, and LDH loci on 11 and 12, changes in the biochemical profiles of the patients with quantitative chromosomal abnormalities cannot be explained by the dosage effect of the structural genes. It is suggested that the marked changes in enzyme activities are due to changes in the interchromosome genic interactions or/and to the dosage effect of the regulatory genes. (16 refs.)

77-4684 **Satellite DNA Organization in the Chromosomes of Primary Cells, L-Cells, and Sarcoma Mouse Cells.** (Eng.) Bianchi, N. O. (Instituto Multidisciplinario de Biologia Celular-IMBICE, Calle 526 entre 10 y 11, C. C. 130, La Plata 1900, Argentina) Bianchi, M. S.; Vidal Rioja, L. A.; Lezana, E. A. *J Natl Cancer Inst* 59(1): 113-118; 1977.

After one cell cycle in 5-bromodeoxyuridine (BUdR), the areas of repetitive DNA in mouse chromosomes showed an asymmetrical distribution of the base analog in the two chromatids. This phenomenon produced a differential Giemsa stain of the sister chromatids in the pericentromeric areas (TC bands) that facilitated cytologic analysis of the organization of repetitive DNA. Primary kidney cells, L cells, and 180 ascites sarcoma cells from BALB/c mice were grown for one cell cycle in BUdR. Some metaphase spreads were tested for C banding; others were processed to induce TC bands. DNA from primary and sarcoma cells was extracted and characterized by ultracentrifugation in CsCl gradients. Primary cells and L cells showed C and TC bands in the centric regions of all chromosomes. Sarcoma cells had C bands in all acrocentric chromosomes and in both arms of a metacentric marker chromosome. TC bands appeared in about half the acrocentrics and in only one arm of the marker chromosome; the other arm and all the remaining acrocentrics lacked TC bands. DNA characterization showed main and satellite bands with the same buoyant density in primary and sarcoma cells. The lack of correspondence between C and TC bands in sarcoma chromosomes may arise by changes in the molecular organization of the repetitive DNA or in the proteins associated with it. (15 refs.)

77-4685 **Experimentally Induced Dysontogenetic Tumors in the Opossum--A Clinicopathological and Histopathological Comparison with Analogous Neoplasms of Man and Other Animals (Meeting Abstract).** (Eng.) Jurgelski, W. (Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC 27709) Hudson, P. M.; Falk, H. L.; Zimmerman, L. E.; Henry, J. M.; Palmer, N. *Proc Am Assoc Cancer Res* 18: 104; 1977. (1 ref.)

77-4686 **Mesenchymal Chondrosarcoma--A Case Report with an Ultrastructural Study and Review of Japanese Literatures.** (Eng.) Mikata, A. (Section Surgical Pathology, Dept. Lab. Medicine, Sch. Medicine, Keio Univ., 35 Shinanomachi, Shinjukuku, Tokyo, Japan); Iri, H.; Inuyama, Y. *Acta Pathol Jpn* 27(1): 93-109; 1977.

A mesenchymal chondrosarcoma occurred in the left maxilla of a 30-yr-old man. Electron microscopy confirmed transition of undifferentiated cells to chondrocytes and calcification. Matrix vesicles were thought to be the cytoplasmic products of tumor chondrocytes. The intercellular matrix contained electron-dense, finely granular deposits resembling the organic matrix of cartilaginous calcification. (20 refs.)

77-4687 **The Lx Bodies of an Eosinophilic Granuloma In Vivo and In Vitro.** (Eng.) Ijuhin, N. (Dept. Oral Pathology, Hiroshima Univ. Sch. Dentistry, Kasumi-Cho, Hiroshima City, Japan); Rose, G. G.; Kobayashi, K.; Mahan, C. J.; Romsdahl, M. M. *Tex Rep Biol Med* 34(2/4): 267-288; 1976.

The ultrastructure of a biopsied and cultured specimen of an eosinophilic granuloma from the humerus of a 19-yr-old male is described. The typical tumor cell in vivo was the generally round histiocyte, containing Langerhans cell-type granules (Lx bodies), lamellar bodies, cytoplasmic clefts, and a markedly indented nucleus. The Lx body was often continuous with the cell membrane, contained a typical periodic or nonperiodic median density, and had dilatations, some of which were coated and similar to membrane-coated vesicles. The longest Lx body measured 4,000 nanometers (nm). After 18 days in culture, the ultrastructure of the histiocytes was similar to that of histiocytes in vivo. However, the Lx body in vitro had no association with the cell membrane, no membrane coating, the median density was usually nonperiodic, and the longest body measured 7,000 nm. Ls bodies in vi
were occasionally associated with vesicles containing me
brane-enclosed particles (70-80 nm in diameter) witho
dense cores, whereas the median density of some Lx bodi
in vitro were associated with membrane-enclosed partic
(42-58 nm in diameter) with dense cores. According to th
small size, uniformity, and membrane-enclosed constructio
these particles are termed virus-like. No particles were fou
in the extracellular spaces. Whether they are integrally i
volved in the etiology or pathogenesis of the histiocytosis-
diseases is not clear. It is postulated that the Langerhans ce
are histiocytes and that the Lx bodies and Langerhans c
granules are the result of endocytosis. The in vitro histiocyt
of the eosinophilic granuloma showed endocytosis that w
marked but not attended by Lx body formation, suggesti
that the in vitro environment did not present the histiocyt
with an Lx body-stimulating factor (Lx SF) and that the
vitro Lx bodies were the result of an endocytosis by the his
ocytes during exposure to an LxSF in vivo. (53 refs.)

77-4688 **Carcinoma Occurring in Rhinophyma (Letter
Editor).** (Eng.) Brubaker, D. B. (Pittsburg
PA) Hellstrom, R. H. *Arch Dermatol* 113(6): 847-84
1977.

The development of a basal cell carcinoma of the nose in
74-yr-old man with rhinophyma is reported. Microscopic e
amination showed that the neoplasm arose directly from t
rhinophyma, which was characterized by fingerlike proje
tions showing severe dysplasia, carcinoma in situ, and ca
cinoma of the basal and basosquamous types. (8 refs.)

77-4689 **Juvenile Nasopharyngeal Angiofibroma: An U
trastructural Study.** (Eng.) Taxy, J. B. (U.
Army Medical Res. Inst. Infectious Diseases, Ft. Detric
Frederick, MD 21701) *Cancer* 39(3): 1044-1054; 1977.

Four clinically and histologically typical juvenile nas
pharyngeal angiofibromas were examined by electron micro
copy. An original tumor and a first, fifth, and sixth recu
rence were studied. The stromal cells of the original and fir
recurrence tumors contained lobulated nuclei, large intran
clear inclusions, variable amounts of rough endoplasm
reticulum (RER) and thin filaments, hemidesmosomes, foc
basal lamina, and prominent pinocytotic vesicles. In the fift
and sixth recurrence tumors, the nuclei often had serrate
margins and smaller inclusions. The cytoplasm containe
dilated cisternae of RER and numerous thin filaments wit
dense bodies. Hemidesmosomes and pinocytosis were dimi
ished; no basal lamina was observed. These observations ind
cate that the stromal cell of this tumor undergoes structur
modulation between its early and late stages. The nucle
granules appear to diminish in size with time. The cells i
both stages possess features common to both fibroblasts an

oth muscle cells. Such a hybridized mesenchyma cell, ie,
ofibroblast, has been previously described for other fibro-
liferative lesions, although its presence in this tumor is of
ertain significance. Additional electron microscopic stu-
of fibrous and soft tissue lesions are needed to character-
the prevalence and origin of the myofibroblast further. (38
.)

4690 **Malignant Fibrous Histiocytoma. An Electron
Microscopic Study.** (Eng.) Taxy, J. B. (Div. Pa-
logy, USAMRIID, Fort Detrick, Frederick, MD 21701)
tifora, H. *Cancer* 40(1): 254-267; 1977.

ultrastructural study of tissue from 15 patients with
lignant fibrous histiocytoma indicates that there are sever-
ypes of histiocytomas and that the histiocyte may repre-
t a morphologic state of a given mesenchymal cell rather
n a particular cell type. The histogenesis is unclear. (48
.)

4691 **Malignant Giant Cell Tumor of Soft Parts. An
Ultrastructural Study of Four Cases.** (Eng.) Al-
cil-Garcia, A. (Mayo Clinic, 200 First St. SW, Rochester,
55901) Unni, K. K.; Goellner, J. R. *Cancer* 40(1): 244-
; 1977.

ultrastructural study of malignant cell tumor of the soft
ts using tissue from four patients indicated that this tumor
mesenchymal sarcoma with monohistiocytic and fibro-
stic differentiation. It also appears to be a distinct subtype
malignant fibrous histiocytoma. (32 refs.)

4692 **Atypical Glycogen Deposits in a Plasmacytoma:
An Ultrastructural Study.** (Eng.) Ghadially, F.
(Dept. Pathology, Univ. Hosp., Univ. Saskatchewan, Sas-
toon, Saskatchewan, Canada, S7N OWO) Lowes, N. R.;
sfin, G. M. *J Pathol* 122(3): 157-162; 1977.

solitary, benign plasmacytoma arising from the gum of the
ver jaw of an 18-yr-old cross-bred terrier dog was studied
light and electron microscopy to record the ultrastructure
this tumor and to probe the significance of atypical glyco-
deposits. The tumor had presented as a red pedunculated
wth about 2.5 cm in diameter. Both light and electron
croscopy established that the tumor parenchyma com-
sed a uniform population of neoplastic plasma cells. A
ominent nucleolus, with associated heterochromatin, was
ually present. Except in rare instances, the characteristic
ckface or cartwheel pattern of heterochromatin was not
dent. As in normal plasma cells, the rough endoplasmic
iculum was abundant, but only rarely were stacks of cister-
e present. In most cells, the cisternae were dilated or
iculated and they frequently contained collections of
noparticulate and rosette forms of glycogen. Monopar-
ulate glycogen deposits were also found in the mitochondria, and they were invariably bounded by a single membrane. However, glycogen particles were not found in the cytoplasmic matrix or in the nucleus. Apparently most, or perhaps all, stages of glycogen synthesis occurred within the mitochondria and rough endoplasmic reticulum of the tumor cells. (12 refs.)

77-4693 **Localization and Organization of Microfilaments and Related Proteins in Normal and Virus-transformed Cells.** (Eng.) Goldman, R. D. (Dept. Biological Sciences, Mellon Inst. Science, Carnegie-Mellon Univ., Pittsburgh, PA 15213) Yerna, M. J.; Schloss, J. A. *J Supramol Struct* 5(2): 155-183; 1976.

Light microscopic, electron microscopic, and biochemical studies of the localization and organization of actinlike microfilaments in normal cells (rat and hamster embryo cells, mouse 3T3 cells), SV40-transformed cells (line SV101), and adenovirus-transformed hamster embryo cells (line 14b) are discussed extensively. In 14b cells, microfilament meshworks appear to be the predominant form of cellular actin, but in normal hamster cells, microfilament bundles are prevalent. In SV101 cells, light microscopy shows that most cells do not possess stress fibers, but electron microscopy reveals that there are as many microfilament bundles in the cytoplasm as in normal 3T3 cells. Most of the microfilament bundles are found in the cortical cytoplasm just beneath the plasma membrane at the adhesive surface of both cell types. The discrepancy between the light and electron microscopic findings is not due to a significant difference in the thickness or number of microfilament bundles. The intracellular arrangement of microfilament bundles may not allow them to be resolved as stress fibers by light microscopy. Attempts at relating the ultrastructural changes in transformed cells to the images obtained following reaction with fluorescein-labeled myosin fragments and indirect immunofluorescence with smooth muscle myosin antibody are discussed. In several instances, the fluorescence microscope images do not correspond to the ultrastructural observations. The results are discussed in terms of the possible relationships between alterations in cytoplasmic contractile elements and the abnormal behavior of transformed cells. (43 refs.)

77-4694 **Surface Morphology of Normal and Neoplastic Rat Cells.** (Eng.) Cloyd, M. W. (Dept. Pathology, Duke Univ. Medical Center, Durham, NC 27710) Bigner, D. D. *Am J Pathol* 88(11): 29-52; 1977.

Nontumorigenic rat cells and their tumorigenic counterparts were studied by scanning electron microscopy under controlled conditions in vitro and by electron microscopy after replantation in vivo to discern if external morphology reflected the cell's neoplastic state or the etiology of transformation. All cell lines were derived from trypsinized embryos, kidneys, or sc tumors of inbred Fischer 344 and BDIX rats. Interphase cells in 6/7 nontumorigenic lines were flat and monolayered under confluent conditions, and they exhibited a smooth, nonactive cell surface. A nontumorigenic cell line morphologically transformed with human adenovirus 2 consisted of spherical cells with blebbed surfaces. Cells from six tumorigenic lines transformed by avian sarcoma virus had highly active surfaces with many surface projections. Cells from rat embryo lines transformed by 3-methylcholanthrene (MC) and 7,12-dimethylbenzanthracene were flat, with no surface projections, in subconfluent culture and rounded, with only a few microvilli, at high densities. In contrast, cells from an MC-induced sarcoma in an adult rat were villous. The villous cells lost most microvilli when they were syngeneically replanted in vivo. The external morphology of cells was influenced by a number of factors simultaneously, with no universal pattern associated with tumorigenic capacity or transforming agent. (65 refs.)

77-4695 **Invasion of Malignant Cells into ^{51}Cr-labeled Host Tissues in Organotypical Culture.** (Eng.) Mareel, M. (Dept. Experimental Cancerology, Clinic Radiotherapy and Nuclear Medicine, Univ. Hosp., De Pintelaan 135, B-9000 Ghent, Belgium) de Bruyne, G.; de Ridder, L. *Oncology* 34(1): 6-9; 1977.

To provide a quantitative assay for the extent of malignant invasion in vitro, an attempt was made to measure the release of ^{51}Cr from prelabeled fragments of embryonic chick heart and mesonephros, cultured either on semisolid or in fluid medium, during their invasion by HeLa cells. Although demonstrated morphologically, malignant invasion did not bring about significant changes in ^{51}Cr release compared to control cultures without HeLa cells. It is suggested that the cytocidal processes associated with malignant invasion may not rupture the plasma membranes of the host tissue cells. (13 refs.)

77-4696 **Histochemical and Ultrastructural Investigations of Invasive Tumor Growth. I. Enzyme Histochemical Investigations.** (Ger.) Hecker, D. (Geschwulstklinik des Medizinischen Bereiches, Humboldt-Universitat, Schumannstrasse 20/21, DDR-104 Berlin, E. Germany) *Acta Histochem (Jena)* 58(1): 105-124; 1977.

Evidence is presented that enzymatic lysis by the infiltrating tumor cells plays an important role in destructive tumor growth. Histochemical studies were carried out on 12 human fibroadenomas, 15 mastopathias, 10 gynecomastias, 18 mammary carcinomas, 20 ovarian carcinomas, 10 malignant melanomas, and 62 transplanted rat tumors as well as in normal tissues. In the mammary and ovarian carcinomas, infiltrating growing tumor areas were characterized by increased activity of NADH diaphorase, NAD-dependent lactate dehydrogenase, glucose-6-phosphate dehydrogenase, isocitric acid dehydrogenase, malate dehydrogenase, acid phosphatase, unspecific esterase, leucine aminopeptidase, and β-glucuronidase. Increased leucine aminopeptidase and increased β-glucuronidase were found near the margin of the transplant tumors. In contrast, there was no indication o specific enzymatic lysis by living cells of the malignant melanomas. Since the enzymatic histochemical findings differ between some human and animal tumors, it cannot always be determined from a model tumor if the results are the rule or an exception. (45 refs.)

77-4697 **Avascular and Vascular Phases of Tumour Growth in the Chick Embryo.** (Eng.) Knighton D. (Dept. Surgery, Children's Hosp. Medical Center, Boston MA) Ausprunk, D.; Tapper, D.; Folkman, J. *Br J Cancer* 35(3): 347-356; 1977.

Tumor diameter and changes in the vasculature in response to Walker 256 carcinosarcoma implants on the chorioallantoic membrane (CAM) of chick embryos (ages 5-16 days) were recorded. Tumors remained avascular for 72 hr, after which they were penetrated by new blood vessels and began rapid growth. This vascular phase decreased the later the day of implantation. (16 refs.)

77-4698 **Marked Instability of Character of Cloned Epithelial Cells.** (Eng.) Schnebli, H. P. (Friedrich Miescher-Institut, Post Office Box 273, CH-4002 Basel, Switzerland) Burger, M.; Strasser, F. F.; Suter, E. *Exp Cell Bio* 45(1-2): 24-33; 1977.

Marked and unexpected changes in the characteristics of cell lines derived from 7,12-dimethylbenzanthracene-induced rat mammary carcinomas occurred when the cells were cultured in vitro. Cloning efficiency, requirement for hydrocortisone and fetal serum, ease of detachment by trypsinization, and chromosomal changes changed progressively with increased number of passages. (11 refs.)

See also:
* (Rev.): 77-4207, 77-4218, 77-4219, 77-4241, 77-4242
77-4243, 77-4244, 77-4245, 77-4246, 77-4247, 77-4248
77-4249, 77-4250, 77-4251, 77-4252, 77-4253, 77-4254
77-4255, 77-4256, 77-4257, 77-4258, 77-4259, 77-4260
77-4261, 77-4262.
* (Chem.): 77-4277, 77-4278, 77-4291, 77-4292, 77-4294
77-4296, 77-4317, 77-4326, 77-4329, 77-4331, 77-4337
77-4343, 77-4345, 77-4347, 77-4348, 77-4358, 77-4404
77-4406, 77-4407, 77-4408, 77-4412, 77-4415, 77-4416
77-4418, 77-4422, 77-4431, 77-4432, 77-4437, 77-4438
77-4439, 77-4452.
* (Phys.): 77-4467, 77-4474, 77-4478, 77-4479, 77-4480
* (Viral): 77-4502, 77-4536.
* (Immun.): 77-4551, 77-4560, 77-4561, 77-4578, 77-4582
77-4583, 77-4594, 77-4595, 77-4600, 77-4602, 77-4604
77-4614.
* (Epid.-Biom.): 77-4699, 77-4701, 77-4704, 77-4713.

77-4699 **Malignant Transformation of Peptic Ulcer in Croatia (1962-1972).** (Cro.) Cicek, J. (Republicki Registar za Rak u Republickom Zavodu za Zastitu Zdravja SR Hrvatske, Rockefellerova 7, 41000 Zagreb, Yugoslavia) *Libri Oncol* 5(3/4): 21-27; 1976.

Data on suspected malignant transformation of peptic ulcer for 1962-1972 are presented. Histologically, of the 459 cases, 8 persons had peptic ulcer, 120 ulcerative carcinoma, 7 ulcer and carcinoma, and 284 had malignant transformation (195 men and 89 women). In the last group, 165 patients were 0-69 yr old. The findings were confirmed pathologically in 2.5% of the cases. The results are compared with those found in the existing literature. (24 refs.)

77-4700 **Colorectal Polyps and Carcinoma in Southern Iran.** (Eng.) Haghighi, P. (Dept. Pathology, Pahlavi Univ. Sch. Medicine, Shiraz, Iran) Nasr, K.; Mohallatee, E. A.; Ghassemi, H.; Sadri, S.; Nabizadeh, .; Sheikholeslami, M. H.; Mostafavi, N. *Cancer* 39(1): 274-278; 1977.

The pattern of colorectal polyps and carcinomas in the Fars province of Iran was investigated through a prospective analysis of autopsy colons and a retrospective review of surgical and autopsy specimens. The frequency of polyps in 801 consecutive autopsies was low (1.56%) compared with that in Hawaii (Japanese immigrants: 60.5%), in the US (33%-51%), and in Australia (20%). The polyps were mostly adenomatous, and they were more common in the colon than in the rectum. Only 2 adenomatous polyps and no hyperplastic polyps were noted in 64,958 surgical specimens obtained from 1952 to 1973. In the period 1963-1973, there were 80 carcinomas of the rectum and 66 of the colon, of which 33 were located in the ascending colon or cecum. The frequency of colorectal carcinomas increased with age up to 54 yr, but it was considerably lower in Fars compared with the US, as represented by Connecticut. (19 refs.)

77-4701 **Gastrointestinal Neoplasia: An Investigative Approach.** (Eng.) Lipkin, M. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021); Deschner, E. E. *In: Genetics of Human Cancer.* Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F. (New York: Raven Press): Progress in Cancer Research and Therapy. 3: 369-375; 1977.

A statistical method of predicting individual susceptibility to gastrointestinal neoplasia is presented, with particular emphasis on colon cancer and its premalignant antecedent pa- hologies. Recent findings suggest that interactions between genetic and environmental factors are involved in cellular changes leading to neoplastic transformation of gastrointestinal epithelial cells. Significant phenotypic traits occurring in high risk population groups are used to estimate the probabilities of cancer development. (26 refs.)

77-4702 **Correlations of Incidence Rates for Selected Cancers in the Nine Areas of the Third National Cancer Survey.** (Eng.) Winkelstein, W. (Dept. Biomedical and Environmental Health Sciences, Sch. Public Health, Univ. California, Berkeley, Berkeley, CA 94720) Sacks, S. T.; Ernster, V. L.; Selvin, S. *Am J Epidemiol* 105(5): 407-419; 1977.

Incidence data from the Third National Cancer Survey were used to study geographic variation in the occurrence of common cancers of nine nonsexual sites and five sexual sites. It was hypothesized that cancers with similar variations in incidence rates in the nine survey communities might have common etiologic factors. The variation was measured by a series of rank and product-moment correlation coefficients in order to summarize the association between pairs of cancers in white men and in white women. The most notable findings were high correlations between the incidence rates for the three gastrointestinal sites (stomach, colon, and rectum) and bladder cancer in both men and women and the high correlation between three female sexual sites (breast, corpus uteri, and ovary). These two clusters are also correlated with one another. Several other substantial correlations between pairs of cancers were observed and discussed. These associations suggest possible common etiologic agents, despite the fact that the individual secular trends for some of these cancers differ. (19 refs.)

77-4703 **Prospects for Population Oncogenetics.** (Eng.) Skolnick, M. (Dept. Medical Biophysics and Computing, Univ. Utah, Salt Lake City, UT 84132). *In: Genetics of Human Cancer.* Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F. (New York: Raven Press): Progress in Cancer Research and Therapy 3: 19-25; 1977.

A review of several studies in progress is presented to demonstrate insights into cancer etiology best derived from population-based studies. In Utah, the large and well-documented Mormon genealogy is being linked to a population-based tumor registry for the study of familial clusters and genetic components of various cancer sites. Preliminary results on 100 melanoma and 135 lip cancer patients are presented. (33 refs.)

77-4704 **The Surgeon, Genetics, and Cancer Control: The Cancer Family Syndrome.** (Eng.) Lynch, H. T. (Dept. Preventive Medicine and Public Health, Creighton Univ. Sch. Medicine, Omaha, NB 68178); Harris, R. E.; Organ, C. H.; Guirgis, H. A.; Lynch, P. M.; Lynch, J. F.; Nelson, E. J. *Ann Surg* 185(3): 435-440; 1977.

Vital cancer statistics and a genetic evaluation are presented for 127 individuals who comprise a family manifesting the cancer family syndrome. Findings include excess of carcinoma of the colon and endometrium, multiple primary cancer, early age of onset, and autosomal dominant mode of genetic transmission. (17 refs.)

77-4705 **The Lognormal Distribution of the Incubation Time of Exogenous Diseases. Genetic Interpretations and a Computer Simulation.** (Eng.) Kondo, K. (Dept. Neurology, Brain Res. Inst., Niigata Univ., Niigata, Japan) *Jpn J Hum Genet* 21(4): 217-237; 1977.

Based on a multifactorial genetic hypothesis, the underlying mechanism of the incubation process and distribution of the incubation time of various classes of diseases were investigated. Under a variety of conditions of the genotypic effect, gene frequency, and threshold, computer simulations indicated that the incubation time for an exposed population to develop a hypothetical disease was noncentrally lognormal in its distribution. Testing of the fits of the theoretical distribution to the observed distributions in various diseases involved the use of epidemic data in a single-exposure cohort that satisfied specific conditions. In addition to several infectious, toxic, and allergic diseases, cases of leukemia induced by radiation in patients with ankylosing spondylitis, leukemia in atomic bomb survivors, thyroid gland cancer induced by radiation treatment of thyroid disease during childhood, and urinary bladder cancer among factory workers exposed to aniline, benzidine, and naphthylamine were tested against the model. All of these induced malignancies fit at the 5% significance level. (49 refs.)

77-4706 **A Few Notes on the Increasing Frequency of Ovarian Cancer.** (Dut.) Hoogendoorn, D. (Centraal Bureau voor de Statistiek, hoofdafdeling Gezondheidsstatistieken, Netherlands) *Ned Tijdschr Geneeskd* 120(49): 2144-2146; 1977.

A study of the mortality rates from ovarian cancer in The Netherlands revealed a steady increase from 9/100,000 to 13/100,000 over the period 1955 to 1974. This rise was particularly pronounced in women >50 yr old, but the rate remained constant or declined slightly for women <50. The reason for this phenomenon is unknown, since it cannot be ascribed to either improved diagnosis or to the increased use of oral contraceptives. (2 refs.)

77-4707 **The Rising Frequency of Hysterectomy: Its Effect on Uterine Cancer Rates.** (Eng.) Lyon, J. L. (Dept. Family and Community Medicine, Univ. Utah Coll. Medicine, Salt Lake City, UT 84132) Gardner, J. W. *Am J Epidemiol* 105(5): 439-443; 1977.

The number of hysterectomies performed in the US increased approx 60% between 1955 and 1973, far in excess of population growth. This has altered the population at risk for uterine malignancies, but published incidence rates do not correct for this effect. Correction factors to estimate the actual population at risk were derived and then applied to uterine cancer rates. Correction for hysterectomy increased incidence and mortality rates for uterine cancer by 20%-45% in any year and changed the time trend by as much as 30% from 1960 to 1973. The effect was greater for endometrial than cervical cancer. Furture studies on uterine cancer occurrence should consider the prevalence of hysterectomized women in the population. (11 refs.)

77-4708 **Exogenous Estrogen and Endometrial Carcinoma: Case-Control and Incidence Study.** (Eng.) McDonald, T. W. (Section Publications, Mayo Clinic, 200 First St., SW, Rochester, MN 55901) Annegers, J. F.; O'Fallon, W. M.; Dockerty, M. B.; Malkasian, G. D.; Kurland, L. T. *Am J Obstet Gynecol* 127(6): 572-580; 1977.

The medical records in Olmsted County, Minnesota, showed a relative risk of endometrial cancer associated with conjugated estrogen treatment of ≥ 6 mo. This risk increased with exposure for ≥ 3 yr and with large doses and continuous administration of the steroids. (35 refs.)

77-4709 **Recent Trends in the Incidence of and Mortality from Endometrial Cancer in Connecticut (Meeting Abstract).** (Eng.) Elwood, J. M. (Connecticut Cancer Epidemiology Unit, Yale Univ., New Haven, CT 06510) Marrett, L. D.; Meigs, J. W.; Flannery, J. T. *Am J Epidemiol* 106(3): 240; 1977. (no refs.)

77-4710 **Endometrial Carcinoma in Women under 40 Years of Age. Comparison of Cases in Oral Contraceptive Users and Non-users.** (Eng.) Silverberg, S. G. (Colorado Regional Cancer Center, 165 Cook St., Denver, CO 80206) Makowski, E. L.; Roche, W. D. *Cancer* 39(2): 592-598; 1977.

Clinical and pathological data from a series of women <40 yr of age with endometrial carcinoma and a positive oral contraceptive history (30 cases) were reviewed and compared

ith data on endometrial carcinoma in young women record-
l in the literature (137 cases) and with a series of 25 cases
curring before the availability of oral contraceptives. Al-
ough sequential contraceptive agents account for <10%
all oral contraceptives taken in England, 20/30 contracep-
ve users had been receiving this type of agent exclusively
predominantly. There was a similar incidence of the vari-
ıs histologic types of endometrial carcinoma among the
ree groups, primarily well-differentiated tumors with a
latively favorable prognosis. The only difference was the
esence of secretory features in 14/29 oral contraceptive us-
s compared with 2/25 nonusers. Clinical and pathological
aging was also predominantly favorable and comparable in
l groups. There were major differences in the clinical pro-
les of sequential users <40 yr of age with endometrial car-
noma and all other patients in this age group with the same
isease. The profile of an obese nulliparous woman with his-
logically documented polycystic ovaries, which occurred in
out half of all cases in nonusers of oral contraceptives or
ers of combined agents, was seen in 5%-15% of patients
king sequential agents. It appears that the latter women
ould not be expected to be at a high risk of developing
ndometrial carcinoma under the age of 40 were it not for
eir contraceptive histories. (18 refs.)

7-4711 **Reproductive Cancer and Hormone Use (Meeting Abstract).** (Eng.) Wigle, D. T. (Health and
/elfare Canada, Ottawa, Ontario, Canada K1A OL2)
race, M. *Am J Epidemiol* 106(3): 233; 1977. (no refs.)

7-4712 **Use of Exogenous Hormones in Women with Malignant and Benign Breast Conditions (1972-
974) (Meeting Abstract).** (Eng.) Burns, P. E. (Dr. W. W.
ross Cancer Inst., Edmonton, Alberta, Canada) May, C.;
audette, L. A.; Lees, A. W.; Grace, M. *Am J Epidemiol*
06(3): 232-233; 1977. (no refs.)

'7-4713 **Breast Cancer Risk and Estrogen Profiles (Meeting Abstract).** (Eng.) Vakil, D. V. (Univ.
oronto, Toronto, Ontario M5S 1A8, Canada) Morgan, R.
V. *Am J Epidemiol* 106(3): 232; 1977. (no refs.)

'7-4714 **Breast Cancer and Fertility Trends in Canada.** (Eng.) Wigle, D. T. (Bureau Epidemiology,
oom 230A, Lab. Centre Disease Control, Health Protection
ranch, Health and Welfare Canada, Ottawa, Ontario K1A
)L2, Canada) *Am J Epidemiol* 105(5): 428-438; 1977.

The age-standardized breast cancer mortality rate for Canadian women increased only slightly during the period 1941-1971. In contrast, the age-standardized breast cancer incidence rate for Saskatchewan women more than doubled during the same period. In the interval 1954-1973, there were significant increases in the age-specific mortality rates for women 50-64 yr old and in the age-specific incidence rates for 5/6 age groups in the 45- to 75-yr range. Breast cancer mortality rates during 1970-1972 varied considerably by province. Age-specific rates in the 30- to 69-yr range were significantly and negatively correlated with the proportions by province of married women first married at age 15-19. In Canada and Saskatchewan, respectively, the age-specific breast cancer mortality and incidence rates for women aged 40-59 yr were significantly and negatively correlated with cohort fertility rates at age 20-24. These data support the hypothesis that early pregnancy protects against breast cancer. The sharp decline in fertility rates since 1960 may result in an increased incidence of breast cancer in the future. (17 refs.)

77-4715 **Breast Cancer and Reserpine Use in a Population of Hypertensive and Normotensive Women (Meeting Abstract).** (Eng.) Farber, M. D. (Univ. California, Los Angeles, CA 90024) Detels, R. *Am J Epidemiol* 106(3): 238; 1977. (no refs.)

77-4716 **Association Between Breast Cancer and Malignant Melanoma (Meeting Abstract).** (Eng.) Schoenberg, B. S. (NINCDS, NIH, Bethesda, MD 20014) Christine, B. W. *Am J Epidemiol* 106(3): 232; 1977. (no refs.)

77-4717 **Melanoma Pattern in Lane County, Oregon (Meeting Abstract).** (Eng.) Morton, W. (Univ. Oregon Health Science Center, Portland, OR 97201) Pohl, D.; Starr, G. *Am J Epidemiol* 106(3): 239; 1977. (no refs.)

77-4718 **An Epidemiological Study of Bladder Cancer (Meeting Abstract).** (Eng.) Howe, G. R. (National Cancer Inst. Canada, Toronto, Ontario, Canada) Chambers, L.; Gordon, P.; Morrison, B.; Miller, A. B. *Am J Epidemiol* 106(3): 239; 1977. (no refs.)

77-4719 **Epidemiologic Characteristics of Brain Tumors in Children (Meeting Abstract).** (Eng.) Gold, E. (Johns Hopkins Univ. Sch. Hygiene and Public Health, Baltimore, MD 21205) Gordis, L.; Tonascia, J. *Am J Epidemiol* 106(3): 240-241; 1977. (no refs.) (no refs.)

77-4720 **Cancer Mortality Among Active California Mormans (Meeting Abstract).** (Eng.) Enstrom, J. E. (Sch. Public Health, Univ. California, Los Angeles, CA 90024) *Am J Epidemiol* 106(3): 239; 1977. (no refs.)

77-4721 **Cancer Incidence in Canadian Hutterites (Meeting Abstract).** (Eng.) Gaudette, L. A. (Alberta Cancer Hosp. Board, Edmonton, Alberta, Canada T6G 1Z2) Holmes, T. M.; Laing, L.; Morgan, K.; Grace, M. *Am J Epidemiol* 106(3): 240; 1977. (no refs.)

77-4722 **Effect of Widowerhood on Prostate Cancer Mortality (Meeting Abstract).** (Eng.) Greenwald, P. (New York State Dept. Health, Cancer Control Bureau, Albany, NY 12237) Kirmss, V.; Burnett, W. S. *Am J Epidemiol* 106(3): 232; 1977. (no refs.)

77-4723 **Occupational Exposure to Benzene. Proposed Standards and Notice of Hearing.** (Eng.) Foster, J. (Dept. Labor, Occupational Safety and Health Admin., Office Public Affairs, Third St. and Constitution Ave., NW, Room N3641, Washington, DC 20210) Bingham, E. *Fed Regist* 42(103): 27452-27478; 1977.

Occupational exposure to benzene should not exceed 1 ppm in air over an 8-hr day, with a 5-ppm ceiling limit. Furthermore, eye and skin exposure should also be limited. Other standards affecting occupational exposure are outlined. (1
refs.)

77-4724 **Acrylonitrile and Human Cancer.** (En
Anonymous (Public Affairs Dept., DuPont C
Wilmington, DE) *Am Ind Hyg Assoc J* 38(8): A46-A47; 197

An epidemiological study has revealed an excess of canc
cases in men exposed to acrylonitrile. The exposure level w
subsequently reduced, and studies are continuing. (no ref

77-4725 **The Comparative Analysis of Cell Populatio
of Enterocytes in Different Parts of the Sm
and Large Intestines in Rats. II. The Rate of Enteroc
Migration. General Conclusion and Discussion.** (Rus.) P
harissky, K. M. (Lab. Experimental Tumors, Res. Inst. O
cology, Leningrad, USSR) Klimashevsky, V. F.; Gushch
V. A. *Tsitologiia* 19(3): 318-328; 1977.

The rate of cell migration from the crypts to the surface lay
of the small and large intestines decreases as the cells n
the mucosa. This is probably due to the configuration of
crypts and villae. The duration of the mitotic cycle was c
culated in the small intestine (11-11.5 hr) and colon (18-
hr). A model of the enterocyte life cycle is proposed. (31 re

See also:
* (Rev.): 77-4201, 77-4202, 77-4203, 77-4204, 77-42
77-4206, 77-4207, 77-4220, 77-4221, 77-4226, 77-42
77-4230, 77-4241, 77-4243, 77-4245, 77-4251, 77-42
77-4253, 77-4254, 77-4255, 77-4256, 77-4258, 77-42
* (Chem.): 77-4310, 77-4330, 77-4337, 77-4338, 77-43
77-4340, 77-4341, 77-4396, 77-4418, 77-4444, 77-44
77-4460.
* (Phys.): 77-4466, 77-4470, 77-4476, 77-4477, 77-44
* (Viral): 77-4507.
* (Immun.): 77-4594.
* (Path.): 77-4616, 77-4650.

77-4726 **Establishment and Characterization of Three Human Cell Lines Derived from Intracerebral Metastatic Tumors.** (Fre.) Maunoury, R. (Laboratoire d'Anatomie-Pathologique, Centre hospitalier Sainte-Anne, 1, rue Cabanis, 75674 Paris Cedex 14, France) *C R Acad Sci [D] (Paris)* 284(11): 991-994; 1977.

Three new human cell lines developed from biopsy material of patients with no previous radio- or chemotherapy are described. Cells were dissociated by trypsinization and cultured in antibiotic-free, enriched RPMI 1640 medium. For each ine, four nude mice were inoculated sc with 2 × 10^7 cells. Cell line SA52 was derived from a breast metastasis. Carbon-dextran assay showed 30 femtomoles (fmol) of estradiol receptors and 14 fmol of progesterone receptors per milligram of protein. All inoculations of this cell line were rejected. Cell line SA72 was derived from an intracerebral metastasis, and it consistently produced tumors similar histologically to the parent tumor (melanoma). Cell line SA87, derived from an intracerebral metastasis, produced tumors in all four animals that were histologically and cytochemically similar to the parent stomach carcinoma. One tumor was very large, with extensive infiltration of the abdominal organs. These three cell lines appear to be uncontaminated, and they are characterized by specific, highly distinctive cytologic markers. (5 refs.)

77-4727 **Establishment and Characterization of a Strain of Human Adrenal Tumor Cells That Secrete Estrogen.** (Eng.) Fang, V. S. (Dept. Medicine, Univ. Chicago, Chicago, IL 60637) *Proc Natl Acad Sci USA* 74(3): 1067-1071; 1977.

A newly established strain of epithelioid cells was derived from a metastatic adrenal adenocarcinoma of a male patient. The clonal cell line, designated Fang-8, has been propagated continuously by serial subculture for 20 mo. The cells resemble the cell structure of the zona reticularis of the human adrenal cortex when viewed by electron microscopy. Since passage 12, the cells showed a characteristic ring-forming property in culture. The cells do not produce testosterone, mineralocorticosteroids, or glucocorticosteroids, but they do produce estrogen. Karyotypic analysis revealed a 100% aneuploid, unstable karyotype in the hyperdiploid stem line. Identification of the Y chromosome was uncertain. It is concluded that Fang-8 represents a new human cell line, unlikely to be contaminated with HeLa strains. (20 refs.)

77-4728 **Comparison of the Growth Properties In Vitro and Transplantability of Continuous Mouse Mammary Tumor Cell Lines and Clonal Derivatives.** (Eng.) Butel, J. S. (Dept. Virology and Epidemiology, Baylor Coll. Medicine, Houston, TX 77030) Dudley, J. P.; Medina, D. *Cancer Res* 37(6): 1892-1900; 1977.

The in vitro growth properties of epithelial cell lines derived from murine mammary tumors were studied and correlated with transplantability in vivo in syngeneic immunocompetent mice. The study involved 5 lines and 12 clonal derivatives established from tumors arising in BALB/c or C3H mice either spontaneously or in response to viral, hormonal, or chemical in vivo stimuli. Most of the cell lines produced C-type virus; one C3H line appeared to respond to glucocorticoid stimulation by an enhanced production of B-type virus. None of the following in vitro growth parameters, which are classic indicators of transformation in fibroblasts, correlated invariably with tumorigenicity in vivo: plating efficiency, saturation density, population-doubling times, colony formation on plastic surfaces, and anchorage-independent growth in methylcellulose. There is a need for the recognition and establishment of different growth criteria applicable to transformation studies with cells of epithelial origin. (39 refs.)

77-4729 **The Effect of Serum on Manifestation of Cell Transformation.** (Rus.) Bershadskii, A. D. (Oncological Scientific Center, Acad. Medical Sciences USSR, Moscow, USSR) Gel'fand, V. I.; Gel'shtein, V. I.; Vasil'ev, Iu. M.; Gel'fand, N. M. *Vestn Akad Med Nauk SSSR* (3): 55-59; 1977.

Factors affecting the in vitro transformation of LSF mouse fibroblasts were studied. In the absence of serum, growth stopped at a cell density of 4.3-4.8 × 10^5 cells/ml in modified Eagle's medium, but in medium containing horned cattle serum, growth stopped at a density of 5.5-6.2 × 10^5 cells/ml. Accumulation of ^{3}H-2-deoxy-D-glucose was five times more intensive in the medium containing serum. In addition, benzo(a)pyrene metabolism was almost completely inhibited in cells growing in serum-containing medium. The amount of nonmetabolized compound after 72 hr of incubation was 90%, compared to 28% in cells growing in the absence of serum. Serum caused marked morphological alterations of the LSF cells; ie, they were poorly spread on the surface, and there was an increased density of villi on the upper cell surface. (23 refs.)

77-4730 **Thermosensitive Step Associated with Transfer of the Ti Plasmid During Conjugation: Possible Relation to Transformation in Crown Gall.** (Eng.) Tempe, J. (Genetique et Amelioration des Plantes, Institut National de la Recherche Agronomique, 78000 Versailles, France) Petit, A.; Holsters, M.; van Montagu, M.; Schell, J. *Proc Natl Acad Sci USA* 74(7): 2848-2849; 1977.

A large genetic element, the Ti plasmid, can be transmitted by a conjugative process from oncogenic strains of *Agrobacterium tumefaciens* to strains that have been cured of the plasmid. Experiments were conducted to show that a thermosensitive step exists in the conjugation and that this step is similar to that found in the transformation of a normal cell to a tumor cell in the crown gall disease of plants. Cultures of donor and receptor strains were mixed in a ratio of 10:1 and incubated at various temperatures (23-37 C) for 48 hr. This bacterial mixture was then harvested and cultured with octopine plus antibiotics. After incubation for 1 wk at 25 C, the colonies were scored. The results show that the conjugative process involved in the transfer of the plasmid, like the transformation process in crown gall disease, is thermosensitive, with the critical temperature at or near 30 C in both instances. Thus, both processes share a common thermosensitive step. If the transformation and the conjugative transfer result from similar mechanisms, it would explain why transformation does not occur above 30 C in crown gall disease. (17 refs.)

77-4731 **Survival of Human Cells in the Aggregate Form: Potential Index of In Vitro Cell Transformation.** (Eng.) Steuer, A. F. (Biotech Res. Labs., Inc., 12601 Twinbrook Parkway, Rockville, MD 20852) Rhim, J. S.; Hentosh, P. M.; Ting, R. C. *J Natl Cancer Inst* 58(4): 917-921; 1977.

The ability of human osteogenic sarcoma (HOS) cells to survive in the aggregate form was studied in relation to their ability to form colonies in soft agar and to induce tumors in nude mice. Nontumorigenic HOS cells, which formed colonies in soft agar, could not survive in the aggregate form. Tumorigenic HOS cell lines derived from cells transformed by Kirsten murine sarcoma virus or N-methyl-N$'$-nitro-N-nitrosoguanidine also formed colonies in soft agar, but they survived and proliferated in the aggregated form. Other cell types were tested with the same results. Aggregation assays may provide an additional, reliable method for predicting the tumorigenic potential of a cell population. (25 refs.)

77-4732 **Survival Differences Exhibited by Normal and Transformed Rat Liver Epithelial Cell Lines in the Aggregate Form.** (Eng.) Steuer, A. F. (Biotech Res. Labs., Rockville, MD 20852) Hentosh, P. M.; Diamond, L.; Ting, R. C. *Cancer Res* 37(6): 1864-1867; 1977.

Estimation was made of the viability of normal and transformed rat liver epithelial cells maintained as aggregates in liquid medium above an agar or agarose base that prevent cell attachment. The number of normal aggregated rat live cells from lines K16, WIRL-3C, and RLL declined rapidl (in 1 day), but transformed cells from lines W8, WIRL/SV and R73/3 survived and proliferated in the aggregate form over the 4-day study period. It is suggested that cell surviva in the aggregate form could serve as a criterion for assessin the in vitro transformation of epithelial cells. (22 refs.)

77-4733 **Putrescine-promoted Mutual Adhesiveness o HeLa Cells from Density-inhibited Suspensio Cultures.** (Eng.) Deman, J. (Dept. Experimental Cancerology, Clinic Radiotherapy and Nuclear Medicine, Academi Clinic, De Pintelaan 135, Ghent 9000, Belgium) Bruyneel E. *J Natl Cancer Inst* 58(1): 145-147; 1977.

The mutual adhesiveness of HeLa cells harvested from density-inhibited suspension cultures was significantly enhance by the addition of putrescine. In contrast, putrescine had n significant effect on the adhesiveness of HeLa cells harveste from fast-growing suspension cultures. The effect on the density-inhibited cells was abolished by pretreating the cells wit neuraminidase. (20 refs.)

77-4734 **Competence of Soluble Cell Extracts as Microtubule Assembly Systems. Comparison o Simian Virus 40 Transformed and Nontransformed Mous 3T3 Fibroblasts.** (Eng.) Wiche, G. (Dept. Biochemistry Univ. California, Berkeley, CA 94720) Lundblad, V. J.; Cole R. D. *J Biol Chem* 252(2): 794-796; 1977.

Extracts from simian virus 40-transformed mouse 3T3 fibroblast cells (SV101) were at least as competent for microtubule assembly under standard conditions as those fro normal mouse BALB/C-3T3 cells. Defects in cytoplasmi microtubule skeletons may be due to transformation-dependent changes in the regulatory mechanisms controllin in vivo microtubule assembly. (12 refs.)

77-4735 **Effect of Colcemide on the Radial Spreading o Fibroblasts in Culture.** (Rus.) Ivanova, O. Yu. (Interfaculty Lab. Mathematical Models in Biology, Moscow State Univ., Moscow, USSR) Komm, S. G.; Vasiliev, Yu. M.; Gelfand, I. M. *Tsitologiia* 19(2): 184-185; 1977.

The effect of demecolcine on the spreading of mouse embryo fibroblastlike cells on a flat glass substrate was studied by time-lapse microcinematography and scanning electron microscopy. On the glass, demecolcine did not prevent the tranition of cells into a well-attached state; however, the time needed for this transition was considerably increased compared with the control cultures. Intermediate stages of spreading demecolcine had the following abnormal features in (1) containing medium: shapes of cytoplasmic outgrowths formed by the cell were altered and their distribution along the cell border appeared less regular; (2) partial detachment of the attached parts of cells occurred frequently; (3) the spreading of various parts of the cells was not correlated. Possible mechanisms of demecolcine action on cell spreading are discussed, and it is suggested that intracellular structures sensitive to demecolcine are essential for coordination of reactions that occur in various parts of the cell during spreading. (12 refs.)

77-4736 **Isolation of Clonal Strains of Chicken Embryo Fibroblasts.** (Eng.) Beug, H. (Max-Planck-Institut fur Virusforschung, Biologisch-medizinische Abteilung, Tubingen, W. Germany) Graf, T. *Exp Cell Res* 107(2): 417-428; 1977.

A method for cloning chicken embryo fibroblasts (CEF) was developed that yields a cloning efficiency of up to 50% without the use of feeder cells or conditioned medium. An analysis of the growth potential of > 200 randomly selected clones showed that only approx 4% of the clones were capable of doubling > 35 times before they underwent cellular senescence. A positive correlation between initial growth rate and in vitro life span was observed. This served as a basis for a similar selection procedure for fibroblast strains suitable for long-term culturing. None of the 200 clones thus isolated could be established into a line. Subclones from clonal CEF strains were more homogeneous than uncloned CEF cultures with respect to morphology and growth behavior, but they were still heterogeneous in their in vitro life span. All fibroblast strains tested were effectively infected and transformed by avian sarcoma viruses of subgroups A, B, C, and D and by avian leukosis virus strains MC29 and REV-ES4. (31 refs.)

77-4737 **Quantitative Studies of Responses of Normal and Transformed Fibroblasts to Oriented Substrates.** (Rus.) Rovenskii, Iu. A. (Oncological Scientific Center, Acad. Medical Sciences USSR, Moscow, USSR) Samoilov, V. I.; Slavnaia, I. L.; Slovachevskii M. S. *Vestn Akad Med Nauk SSSR* (3): 59-61; 1977.

The quantitative evaluation of contact orientation of fibroblasts in culture is described. Normal human rat, mouse, and hamster fibroblasts and various transformed fibroblasts were grown on a surface with a specifically oriented contour. Normal fibroblasts responded to the increase of surface curvature by a corresponding elongation of the cell nucleus, but transformed fibroblasts lacked this ability. (no refs.)

77-4738 **Role of Surface Modulating Assemblies in Growth Control of Normal and Transformed Fibroblasts.** (Eng.) McClain, D. A. (Rockefeller Univ., New York, NY 10021) D'Eustachio, P.; Edelman, G. M. *Proc Natl Acad Sci USA* 74(2): 666-670; 1977.

Cellular microtubules, microfilaments, and surface receptors have been postulated to form a surface modulating assembly (SMA) that regulates surface receptor mobility and cell growth. To test this hypothesis, three agents known to affect cell growth [colchicine, concanavalin A (Con A), and the src gene product of Rous sarcoma virus] were examined for their effects on chick embryo fibroblasts. Colchicine blocked the entry of cells into the S phase, as did Con A when present in doses sufficient to modulate surface receptor mobility. Succinyl-Con A, which does not induce surface modulation, had no effect. Both Con A and colchicine blocked the appearance of cytoplasmic factors capable of stimulating DNA replication in a cell-free system. To study the endogenous effects on the SMA, the fibroblasts were infected with a Rous sarcoma virus (*ts*NY68) having a temperature-sensitive mutation in the transforming (*src*) gene. *Ts*NY68-infected fibroblasts shifted to the nonpermissive temperature acquired normal microtubular morphology more rapidly (2 hr) than cells grown at the permissive temperature in the presence of protein synthesis inhibitors (7.5 hr). This suggests that the *src* gene product acts directly on the SMA rather than via the nucleus or at the level of protein synthesis. Furthermore, transformation of the SMA was partly blocked by treatment of the infected cell with Con A but not succinyl-Con A. Both Con A and colchicine inhibited entry into the S phase following a shift from nonpermissive to permissive growth conditions. These observations are in accord with the hypothesis that the SMA acts as a signal regulator in growth control. (14 refs.)

77-4739 **Surface Properties of Mouse Mammary Cells (Meeting Abstract).** (Eng.) Asch, B. B. (Dept. Cell Biology, Baylor Coll. Medicine, Houston, TX 77030) *Proc Am Assoc Cancer Res* 18: 24; 1977. (no refs.)

77-4740 **The Metabolic Effects and Uptake of Ethidium Bromide by Rat Liver Mitochondria.** (Eng.) Pena, A. (Departamento de Biologia Experimental, Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Apartado Postal 70-600, Mexico 20, D. F.) Chavez, E.; Carabez, A.; Tuena de Gomez-Puyou, M. *Arch Biochem Biophys* 180(2): 522-529; 1977.

The uptake of ethidium bromide (EB) by rat liver mitochondria and its effect on mitochondria, submitochondrial particles, and F_1 (prepared from beef heart submitochondrial particles) were studied. EB inhibited the State 4-State 3 transition with glutamate or succinate as substrates. With glutamate, EB did not affect State 4 respiration, but with succinate it induced max respiration. Both the stimulation of State 4 respiration and the inhibition of State 3 respiratory rates were concentration-dependent. The uptake of EB by the mitochondria appears to be an energy-requiring process; the use of endogenous substrates apparently suffices to support uptake of the dye. In submitochondrial particles, the aerobic oxidation of NADH in the presence of K+ was much more sensitive to EB than that of succinate. EB partially inhibited the ATPase activity of submitochondrial particles and the F_1 preparation. The accumulation of the dye by the mitochondria may explain why EB acts as an inhibitor of oxidative phosphorylation. Upon accumulation of high amounts of EB, inhibition of ATPase would occur, and this might contribute to the inhibition of State 3 respiration. The ability of mitochondria to concentrate EB may also be involved in the selectivity of the dye as a mitochondrial mutagen. (18 refs.)

77-4741 **Epigenetic Variation of Cultured Somatic Cells: Evidence for Gradual Changes in the Requirement for Factors Promoting Cell Division.** (Eng.) Meins, F. (Dept. Botany, Univ. Illinois, Urbana, IL 61801) Binns, A. *Proc Natl Acad Sci USA* 74(7): 2928-2932; 1977.

Classic breeding experiments using totipotent plant cells were used to study cytokinin habituation, a type of heritable change that can be induced and reversed under precisely defined culture conditions, and its relationship to tumor progression. Cytokinin habituation occurs when plant cells in culture lose their requirement for an exogenous supply of cell division factor and are able to produce this factor themselves. Cell lines were obtained from pith parenchyma explants of tobacco (*Nicotiana tabacum*). For the habituation assays, explants of clones were incubated in basal medium or basal medium supplemented with kinetin. Habituation is expressed at the ratio of tissue-doubling constants on media without and with kinetin. Habituation was found to be gradual rather than an all-or-none process that led to progressively more autotrophic tissues. Cells showed reversible shifts among a range of habituated states, but they remained totipotent and capable of reverting to the cytokinin-requiring phenotype. Thus, habituation apparently involves epigenetic changes in a quantitiative cellular phenotype. The findings support the hypothesis that tumor progression in crown gall, a neoplastic disease of higher plants, can be accounted for by heritable changes in the pattern of gene expression. (34 refs.)

77-4742 **Vegetative Reproduction by Budding in Hydra: A Perspective on Tumors.** (Eng.) Shostak, S. (Dept. Life Sciences, Univ. Pittsburgh, Pittsburgh, PA 15260) *Perspect Biol Med* 20(4): 545-568; 1977.

Findings obtained by studying the coelenterate, *Hydra viridis*, have been applied to tumor growth and metastases. Particular attention is focused on cell feed-in, cell feed-out, and cell feed-out and tumo metastases. (98 refs.)

77-4743 **Tumor Development in Malnourished Guinea Pigs (Meeting Abstract).** (Eng.) Weeks, B. A. (Univ. South Carolina Sch. Medicine, Columbia, SC 29208) *Proc Am Assoc Cancer Res* 18: 36; 1977. (no refs.)

77-4744 **Free Radicals During the Growth of Transplanted Pigmented Melanoma.** (Rus.) Bogdanov, G. N. (Inst. Chemical Physics, Acad. Sciences USSR, Chernogolovka, Moscow Oblast', USSR) Varfolomeev, V. N.; Pavlovskii, I. V.; Vasil'eva, L. S.; Goloshchapov, A. N.; Emanuel', N. M. *Dokl Akad Nauk SSSR* 233(2): 494-497; 1977

Electron paramagnetic resonance was used to study the distribution and content of free radicals in Harding-Passey melanomas transplanted in C3HA mice. The concentration of free-radical centers in the pigmented tumor showed a characteristic increase up to day 16 after tumor transplantation. On day 18, a further increase was noted. This second increase in free-radical concentration was possibly due to secondary processes in the melanoproteins. The content of free radicals in the center of the tumor was significantly higher than that in the peripheral region. (8 refs.)

77-4745 **Pterin-6-aldehyde, a Cancer Cell Catabolite: Identification and Application in Diagnosis and Treatment of Human Cancer.** (Eng.) Halpern, R. (Dept. Chemistry, Univ. California, Los Angeles, CA 90024) Halpern, B. C.; Stea, B.; Dunlap, A.; Conklin, K.; Clark, B. Ashe, H.; Sperling, L.; Halpern, J. A.; Hardy, D.; Smith R. A.; *Proc Natl Acad Sci USA* 74(2): 587-591; 1977

The active degradation by human cancer cells in tissue culture of folic acid, with the concomitant formation and excretion of pterin-6-aldehyde, is reported. Adult normal fibroblasts and epithelial cells, amniotic cells, and embryonic cells did not degrade folic acid to a measurable degree. When urine from 29 patients was analyzed by thin-layer chromatography, pterin-6-aldehyde (> 300 nanomoles) was found only in the urine of the 13 patients with a tissue diagnosis of cancer. After total resection of the neoplasm, the compound was no longer present in the urine. Pterin-6-aldehyde is not excreted by healthy patients unless their diets are supplemented with folic acid. (17 refs.)

77-4746 **Differential Effects of Chemical Inducers on Expression of β Globin Genes in Murine Erythroleukemia Cells.** (Eng.) Nudel, U. (Dept. Medicine, Columbia Univ., New York, NY 10032) Salmon, J. E.; Terada, M.; Bank, A.; Rifkind, R. A.; Marks, P. A. *Proc Natl Acad Sci USA* 74(3): 1100-1104; 1977.

The effect of inducers of erythroid differentiation, such as dimethyl sulfoxide (DMSO), hexamethylene bisacetamide (HMBA), butyric acid, and propionic acid, on the expression of two β globin genes, βmaj and βmin, during the differentiation of murine erythroleukemia cells was examined. After 4 days of culture of murine erythroleukemia cells with HMBA or DMSO, the βmaj-containing Hb (Hbmaj) predominated. In the presence of butyric or propionic acid and after 4 days of culture, relatively equal amounts of Hbmaj and Hbmin were found. When cultured with DMSO or HMBA, murine erythroleukemia cells synthesized more βmaj than βmin, but equal amounts were synthesized in the presence of butyric acid. When poly(A)-containing RNA from the cells exposed to different inducers was translated in a wheat germ cell-free system, the ratio of βmaj to βmin synthesized reflected that in whole cells. In a strain of murine erythroleukemia cells resistant to DMSO (DR-10), the preferential stimulation of βmaj synthesis by HMBA and of βmin synthesis by butyric acid was more pronounced than with the DMSO-sensitive cells. These results suggest that polar compounds and fatty acids cause different expression of the βmaj and βmin genes in murine erythroleukemia cells. The findings also suggest that the differences in relative amounts of the β globins observed with different types of inducing agents are not attributable to translational or posttranslational regulatory mechanisms. The inducers appear to act directly or indirectly to control the synthesis rates of βmaj and βmin globins by affecting the transcription or processing of messenger RNA for these proteins. (30 refs.)

77-4747 **Nerve Growth Factor Receptors on Human Melanoma Cells in Culture.** (Eng.) Fabricant, R. N. (Lab. Viral Carcinogenesis, NCI, NIH, Bethesda, MD 20014) De Larco, J. E.; Todaro, G. J. *Proc Natl Acad Sci USA* 74(2): 564-569; 1977.

Purified mouse nerve growth factor (NGF) radiolabeled with ^{125}I was tested for its ability to bind to a variety of different cultured cells. NGF bound readily to human and hamster melanoma cells, but not to many other cell lines. The three cell lines with the highest number of NGF receptors were derived from metastatic melanomas. One of these lines, A875, was studied in detail and was shown to have approx 7 x 10^5 NGF receptors/cell with an association constant of 1.0 x 10^9 liters/mole. The use of these cells in competition binding assays permitted the detection of 0.25 nanograms of NGF in various biologic fluids. NGF increased the survival, but not the division, of melanoma cells maintained in medium depleted of serum growth factors. This effect of NGF as a specific "survival factor" appears analogous to its effect on cultured sympathetic ganglion cells and on other cells derived from the neural crest. (25 refs.)

77-4748 **Glycosaminoglycans in Human Lung Carcinoma.** (Eng.) Hatae, Y. (Biochemical Lab., Cancer Inst., Hokkaido Univ. Sch. Medicine, Kita-15-jo, Nishi-7-chome, Kita-ku, Sapporo 060, Japan); Atsuta, T.; Makita, A. *Gann* 68(1): 59-63; 1977.

Glycosaminoglycans from human lung squamous cell carcinoma and adenocarcinoma and from normal tissues were characterized chemically, enzymatically, and electrophoretically. There were higher levels of oversulfated chondroitin and/or dermatan sulfates in carcinomatous than in control tissues. Levels of whole glycos aminoglycans, predominantly chondroitin-4-sulfate, chondroitin-6-sulfate and hyaluronic acid, were markedly elevated in lung tumor tissue. (20 refs.)

77-4749 **Gangliosides of Hepatoma 27 and of the Liver in Rats.** (Rus.) Diatlovitskaia, E. V. (M. M. Shemiakin Inst. Bioorganic Chemistry, Acad. Sciences USSR, Moscow, USSR) Novikov, A. M.; Bergel'son, L. D. *Vestn Akad Med Nauk SSSR* (3): 46-50; 1977.

The distribution of gangliosides in normal liver tissue, rapidly growing hepatoma 27, and regenerating (posthepatectomy) liver tissue was studied. The content of lipid-bound sialic acids was significantly increased in the hepatoma cells (1.8 nanomoles/mg, compared to 0.5 nanomole/mg in the normal liver cells). The biosynthesis of sialoglycolipids was slightly inhibited in regenerating liver cells with max inhibition being observed 24 hr after hepatectomy (0.42 nanomole/mg). Upon thin-layer chromatography, five ganglioside fractions were observed in both normal liver cells and regenerating liver cells, but only four fractions were detected in the hepatoma cells. Trisialosylganglioside concentration was markedly elevated in the plasma membranes of the regnerating liver tissue (27%) but this ganglioside was practically absent in the hepatoma cells. (11 refs.)

77-4750 **The Dissociation of the Surface Architecture Described by Enhanced Lectin Agglutinability and the Transformed Phenotype Expressed As Anchorage Independence.** (Eng.) Noonan, K. D. (Dept. Biochemistry and Molecular Biology, J. Hillis Miller Health Center, Univ. Florida, Gainesville, FL 32610) Bouck, N.; di Mayorca, G. *J Cell Physiol* 91(2): 201-208; 1977.

Agglutinability with concanavalin A (Con A) and wheat germ agglutinin (WGA) and growth in semisolid medium were measured in a series of cold-sensitive variants of chemically transformed BHK-21 cells (which display a normal phenotype at 32° and a transformed phenotype at 38°), in revertants to the normal phenotype from a dimethylnitrosamine-transformed clone of BHK-21, and in revertants to the normal phenotype derived from polyoma-transformed BHK-21 cells. There was no correlation between surface architecture, as detected by Con A and WGA, and the ability of these cell lines to express the transformed phenotype defined by growth in semisolid medium. Thus, temperature-sensitive variants can maintain the agglutinable surface architecture at both the permissive and nonpermissive temperature, and revertants to the normal phenotype can remain maximally agglutinable, even though they have lost the property of anchorage independence. (28 refs.)

77-4751 **On Cell Membrane Lipid Fluidity and Plant Lectin Agglutinability. A Spin Label Study of Mouse Ascites Tumor Cells.** (Eng.) Bales, B. L. (Centro de Fisica, I.V.I.C., Apartado 1827, Caracas, Venezuela) Lesin, E. S.; Oppenheimer, S. B. *Biochim Biophys Acta* 465(2): 400-407; 1977.

The plasma membrane fluidity of Sarcoma 180 mouse ascites tumor cells was investigated. The results showed a similarity to the membrane fluidity of most other mammalian cells. There was no measurable correlation between lipid fluidity and agglutinability. (42 refs.)

77-4752 **A Phospholipid Derivative of Cytosine Arabinoside and Its Conversion to Phosphatidylinositol by Animal Tissue.** (Eng.) Raetz, C. R. (Dept. Biochemistry, Coll. Agricultural and Life Sciences, Univ. Wisconsin, Madison, WI 53706) Chu, M. Y.; Srivastava, S. P.; Turcotte, J. G. *Science* 196(4287): 303-305; 1977.

The synthesis of an analog of cytosine diphosphate diglyceride is described in which cytosine arabinoside is substituted for the cytidine moiety. The cytotoxicity and metabolic uniqueness of this compound suggest that similar compounds may be useful in cancer research. (20 refs.)

77-4753 **Regulation of Cholesterol Biosynthesis by Normal and Leukemic (L_2C) Guinea Pig Lymphocytes.** (Eng.) Philippot, J. R. (Tufts-New England Medical Center, Therapeutic Radiology Dept., Radiobiology Div., 171 Harrison Ave., Boston, MA 02111) Cooper, A. G.; Wallach, D. F. *Proc Natl Acad Sci USA* 74(3): 956-960; 1977.

The mechanism(s) responsible for defective regulation of cholesterol biosynthesis in guinea pig leukemic (L_2C) lymphocytes was investigated. L_2C lymphocytes synthesize cholesterol at 30-40 times the rate for normal cells and fatty acids at 20-30 times the normal rate. The increased cholesterol synthesis correlates with an important enhancement of hydroxymethylglutaryl (HMG)-CoA reductase activity and an accumulation of cholesterol in the cells. Exposure of L_2C cells to cholesterol/lecithin liposomes did not depress their sterol biosynthesis. However, 25-hydroxycholesterol, an inhibitor of HMG-CoA reductase, and 25-hydroxycholecalciferol, a biologically potent form of vitamin D, blocked sterol biosynthesis of both normal and L_2C lymphocytes. Both normal and L_2C cells exchanged cholesterol equivalently with cholesterol/lecithin liposomes. The only difference in sterol biosynthesis observed between normal and L_2C cells was in the temperature response of the enzyme. Arrhenius plots of this enzyme activity exhibited a prominent discontinuity at 24 C for normal cells but none for L_2. The activation energies for L_2C cells and normal cells above the normal cell transition temperature were not significantly different. These data suggest that the defective regulation of cholesterol biosynthesis in L_2C lymphocytes may derive from an abnormal constitution of their internal membranes. (30 refs.)

77-4754 **Carbohydrate Metabolism of Tumors and Stage of Tumor Progression.** (Rus.) Gorozhanskaia, E. G. (Oncological Scientific Center, Acad. Medical Sciences USSR, Moscow, USSR) Liubimova, N. V.; Shapot, V. S. *Vestn Akad Med Nauk SSSR* (3): 6-11; 1977.

Carbohydrate metabolism was studied in o-aminoazotoluene-induced hepatomas in C3HA mice and in various human tumors (cancer of the stomach, lung, uterus, and breast, and benign tumors of the lung and uterus). Glucose content, hexokinase (HK) activity, and anaerobic glycolysis rate were assessed quantitatively. Glucose was practically absent in malignant hepatomas 61, 22A, 60, and 40 but was present in relatively benign, slowly growing hepatoma 49 (range, 1.0-3.6 mg/g, compared to 3.3-5.0 mg/g in normal liver tissue). The same tendency was observed in human tumors: glucose was not detected in malignant tumors, but was found in benign tumors (0.08-0.22 mg/g vs 0.17-1.04 mg/g in normal lung, kidney, and stomach tissue). The anaerobic glycolysis rate (micrograms of lactic acid/milligram of protein or dry tissue/hour) was significantly higher in the malignant tumors: 129.7 in hepatoma 22A, 104.1 in hepatoma 61, 96.6 in hepatoma 49, and 34.7 in normal tissue. Accordingly, this rate was 39.9 in stomach cancers, 69.8 in lung cancer, 28.0 in uterine cancer, 29.3 in breast cancer, 17.5 in benign uterine tumor, and 36.6 in benign lung tumor (compared to 5.3 in normal lung tissue and 20.5 in normal kidney tissue). Activity of HK (in nanomoles of glucose/milligram of protein) was significantly elevated in all malignant hepatomas (4.51 in hepatoma 22A, 3.32 in hepatoma 61, and 2.25 in hepatoma 49, compared to 1.12 in normal liver tissue), and in malignant human tumors (1.8, stomach; 2.6, lung; 1.6, uterus; and 1.6, breast, compared to 0.56-1.27 in normal tissues). (20 refs.)

77-4755 Transplantable Thyroid Tumour in Rats: Iodoamino Acid Distribution in Successive Tumour Generations. (Eng.) Volpert, E. M. (Nuclear Medicine Service, Veterans Admin. Hosp., 800 Poly Place, Brooklyn, NY 11209) Prezyna, A. P. *Acta Endocrinol (Kbh)* 85(1): 93-100; 1977.

Dependent and autonomous thyroid tumors were studied biochemically. Fischer 344 female rats were injected with 3 μCi ^{131}I and placed on low-iodine diets (LID) for at least 10 mo before sacrifice and transplantation of their goiters into radiothymectomized rats. The donors were also kept on LID. Four mo after transplantation, several tumors had reached a size large enough for further transplantation. The take was 2/22 tumors when donors had been fed LID 10 mo and 8/22 when the period was increased to 12 mo. These second-generation tumors were transplanted further into intact and radiothymectomized rats. Third-generation tumors were transplanted only into intact rats fed a normal diet. All first-generation thyroid tumors were functional, containing MIT, DIT, T_4, T_3, and, in some cases, 3,3′,5′-triiodothyronine (T′). All fourth-generation tumors were nonfunctional. Second- and third-generation tumors were biochemically unpredictable, some containing all the iodoamino acids, including T′, and others only MIT, I-, and a trace of DIT. The degrees of dedifferentiation and autonomy did not necessarily correlate with loss of function. The results suggest that there are nodules with differing biochemical properties within individual tumors and that T′-secreting nodules will be found. (17 refs.)

77-4756 Regulation of Amino Acid Transport Activity and Growth Rate of Animal Cells in Culture. (Eng.) Oxender, D. L. (Dept. Biological Chemistry, Univ. Michigan, Ann Arbor, MI 48109) Lee, M.; Cecchini, G. *J Biol Chem* 252(8): 2680-2683; 1977.

An increase in cellular amino acids was associated with a decrease in the transport activity of System A and an increase in the activity of System L. Altering cellular amino acids produced a greater response from System L than for System A. The role of these systems in neoplastic transformation is discussed. (30 refs.)

77-4757 High Resolution Proton Magnetic Resonance Spectral Characteristics of Water, Lipid, and Protein Signals from Three Mouse Cell Populations. (Eng.) Block, R. E. (Papanicolaou Cancer Res. Inst. at Miami, Inc., 1155 Northwest 14th St., Box 236188, Miami, FL 33123) Maxwell, G. P.; Prudhomme, D. L.; Hudson, J. L. *J Natl Cancer Inst* 58(1): 151-156; 1977.

The high-resolution proton magnetic resonance spectral properties of three C57BL/6J mouse cell populations (EL 4 ascites tumor cells, normal spleen WBC, and normal RBC) were investigated. Packed cell pellets were investigated at 100 and 13.56 megahertz (MHz). The 100-MHz spectra contained identifiable nonwater proton resonances as well as the water resonance. The major nonwater resonances from the EL 4 cells and normal WBC resembled resonances from lipid extracts, whereas the nonwater resonances from RBC resembled resonances from HB solutions. The reciprocals of the water proton spin-lattice relaxation times were roughly proportional to the total sample water content at both 100 and 13.56 MHz. The estimated slopes of these plots were frequency-dependent. The water proton relaxation rate generally increased with increasing total protein content of the packed cell pellets. (28 refs.)

77-4758 Changes in the Collagenolytic Activity Released by Primary VX-2 Carcinoma Cultures as a Function of Tumor Growth. (Eng.) Dabbous, M. K. (Dept. Biochemistry, Univ. Tennessee Center Health Sciences, Memphis, TN 38163) Sobhy, C.; Roberts, A. N.; Brinkley, B. *Mol Cell Biochem* 16(1): 37-42; 1977.

Collagenolytic activity in the serum-free media of cultures of rabbit VX-2 carcinoma was studied along with change in the chromatographic behavior of this activity as a function of both time in culture and stage of tumor progression. Collagenolytic activity was assessed by the release of soluble radioactive peptides from radiolabeled collagen fibrils and by the reduction in viscosity of acid-soluble collagen solutions consequent upon cleavage of tropocollagen molecules. Three chromatographic fractions of collagenolytic activity were separated by gel filtration: F1, molecular wt 85,000-110,000 daltons, which was present in larger amounts in early cultures of younger tumor tissue; F2 (35,000-40,000 daltons), the major component, with max production in day 3 media of both younger and advanced tumor tissues; and F3 (18,000-22,000 daltons), a minor component. Early cultures of younger tumor tissue contained a latent collagenase that was subject to activation with trypsin. This suggests the presence of enzyme precursors or of enzyme-inhibitor complexes. (22 refs.)

77-4759 Quantitation of a Transformation-sensitive, Adhesive Cell Surface Glycoprotein. Decrease on Several Untransformed Permanent Cell Lines. (Eng.) Yamada, K. M. (Molecular Biology, NCI, NIH, Bethesda, MD 20014) Yamada, S. S.; Pastan, I. *J Cell Biol* 74(2): 648-654; 1977.

The LETS glycoprotein was found to constitute a small amount of the total protein on several continuous untransformed cell lines, in contrast to the higher content on embryonic and early adult passage cells. This decrease is similar to that observed during the course of malignant transformation. (30 refs.)

77-4760 **Characterization of C-reactive Protein and the Complement Subcomponent C1t as Homologous Proteins Displaying Cyclic Pentameric Symmetry (Pentraxins).** (Eng.) Osmand, A. P. (Dept. Immunology, Rush Medical Coll., Chicago, IL 60612) Friedenson, B.; Gewurz, H.; Painter, R. H.; Hofmann, T.; Shelton, E. *Proc Natl Acad Sci USA* 74(2): 739-743; 1977.

Partial amino acid sequences of rabbit C-reactive protein, a peptide derived from human C-reactive protein by cyanogen bromide cleavage, and the C1t subcomponent of the human complement component C1 were determined. The extensive sequence homology between these proteins established their evolutionary relationship. In addition, examination of C-reactive proteins by negative-stain electron microscopy revealed that the protein is composed of five subunits arranged in cyclic symmetry. This structure is similar to that reported for both the C1t glycoprotein and the amyloid P component. The extensive structural relationship suggests similar or overlapping functions, and the term pentraxin is proposed to describe these homologous proteins. (32 refs.)

77-4761 **Metabolically Labeled Cell Membrane Proteins in Spontaneously and In SV40 Virus Transformed Mouse Fibroblasts.** (Eng.) Coll, J. M. (Instituto Nacional De Prevision, Clinica Puerta De Hierro, Bioquimica Experimental, San Martin de Porres, 4, Madrid-35, Spain) Luborsky, S. W.; Mora, P. T. *Biochemistry* 16(14): 3169-3177; 1977.

The relationship between cell-membrane protein composition and cell growth properties was studied in normal, nontumorigenic AL/N mouse embryo fibroblast cells and in derivative simian virus 40 (SV40) or spontaneously transformed cells. In membrane preparations from exponentially growing normal cells, one glycoprotein component (molecular wt approx 250,000) was observed that was consistently reduced or absent in an SV40-transformed cell line. No such compositional difference was observed in a spontaneously transformed tumorigenic clonal derivative cell line or in subclones of such a derivative cell line, with or without SV40 virus infection. However, in metabolic labeling experiments with ^{14}C-labeled mixed amino acids, a consistent decrease was also demonstrated in the biosynthesis of the same protein in the SV40 virus-infected subclone, compared with an uninfected sister subclone, during exponential growth. This specific difference in biosynthesis is apparently related to the presence and functioning of the SV40 gene. It correlates with the ability of these cells to grow in viscous medium, but not with cellular tumorigenicity. (38 refs.)

77-4762 **Restoration of Normal Morphology, Adhesion and Cytoskeleton in Transformed Cells by Addition of a Transformation-sensitive Surface Protein.** (Eng.) Ali, I. U. (Center Cancer Res., Massachusetts Inst. Technology, Cambridge, MA 02139) Mautner, V.; Lanza, R.; Hynes, R. O. *Cell* 11(1): 115-126; 1977.

The effects of the addition of large, external, transformation-sensitive (LETS) glycoprotein on NIL cells transformed by herpes simplex virus (NIL-HSV cells) were evaluated. LETS protein, a major component of the surface of normal cells that is not found in their transformed counterparts, was isolated from both early passage chick embryo fibroblasts and from a cloned line of hamster fibroblasts (NIL cells). Addition of LETS protein altered the morphological characteristics of the NIL-HSV cells to those of untransformed cells. LETS protein attached to the surface of the cells was detected both by iodination and by immunofluorescent staining; the surface distribution detected by immunofluorescence was strikingly similar to that seen in normal cells. The cells also exhibited well-defined actin cables that could not be seen prior to treatment. All of the alterations brought about by the addition of LETS protein could be blocked by pretreatment of LETS protein with antisera or with trypsin. The results suggest that LETS protein has a role in cell attachment and spreading and that it affects the organization of the cytoskeleton. The high rate of uptake of 2-deoxyglucose, a characteristic of transformed cells, was not affected by the addition of LETS protein to the NIL-HSV cells. (44 refs.)

77-4763 **Extensive Disulfide Bonding at the Mammalian Cell Surface.** (Eng.) Hynes, R. O. (Center Cancer Res. Massachusetts Inst. Technology, Cambridge, MA 02139) Destree, A. *Proc Natl Acad Sci USA* 74(7): 2855-2859; 1977.

The extent of intermolecular and intramolecular disulfide bonding among cell-surface proteins of hamster NIL8 cells and hamster sarcoma virus (HSV)-transformed NIL8-HSV cells was studied by lactoperoxidase-catalyzed iodination and sodium dodecyl sulfate/polyacrylamide gel electrophoresis in two dimensions, one prior to and one subsequent to reduction of disulfide linkages. The LETS (large external transformation-sensitive) protein of the NIL8 cell surface was almost exclusively in disulfide-linked complexes, with homodimers being the most prevalnet species. Other cell surface proteins were involved in both intra- and intermolecular disulfide bonding. The LETS protein and certain other disulfide-linked proteins were not seen in the NIL8-HSV cells. (40 refs.)

77-4764 **The Presence of High Mobility Group Nonhistone Chromatin Proteins in Isolated Nucleosomes.** (Eng.) Goodwin, G. H. (Chester Beatty Res. Inst., Inst. Cancer Res., Royal Cancer Hosp., Fulham Road, London SW3 6JB, England) Woodhead, L.; Johns, E. W. *FEBS Lett* 73(1): 85-88; 1977.

The presence of high-mobility group (HMG) nonhistone chromatin proteins was demonstrated in nucleosomes that had been isolated by gel-filtration chromatography following nuclease digestion of rabbit thymus nuclei. Since HMG proteins are susceptible to proteolytic degradation, rabbit thymus was used as it has lower levels of proteolytic enzymes than calf thymus. For comparison, however, polyacrylamide gel electrophoresis (PAGE) patterns of both rabbit and calf thymus proteins, prepared by 0.35 M NaCl extraction, are included. The patterns showed that there are basically only four main proteins, HMG1, HMG2, HMG14, and HMG17, in each thymus. Some histone H1 was also found. The HMG proteins were extracted from monomer nucleosomes and from the total nuclear digest by extraction with 5% perchloric acid. Again, PAGE showed that all four proteins are present in the monomer, along with some histone H1. By comparing the staining intensity of gels of both rabbit thymus and monomer nucleosome HMG proteins, the amount of total HMG proteins in the monomer nucleosome was estimated. The total was calculated to be about 3% of the DNA in the monomer peak, corresponding to the amount of total HMG proteins that can be isolated from whole thymus nuclei. According to PAGE, the size of the DNA in the monomer peak was 150-160 base pairs. This value is smaller than the 200 base-pair repeat; ie, 40-50 base pairs were removed during digestion. All five histones were present on the monomer, although histone H1 was reduced; some H1 was probably lost as the DNA was reduced from 200 to 150-160 base pairs. (19 refs.)

77-4765 **Appearance of a Chromatin Protein During the Erythroid Differentiation of Friend Virus-transformed Cells.** (Eng.) Keppel, F. (Dept. Molecular Biology, Univ. Geneva, 30, quai Ernest-Ansermet, 1211 Geneva 4, Switzerland) Allet, B.; Eisen, H. *Proc Natl Acad Sci USA* 74(2): 653-656; 1977.

Chromatin proteins from erythroleukemia cells transformed by Friend virus were analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. A new chromosomal protein, with an apparent molecular wt of 25,000, appeared during the dimethyl sulfoxide- or hexamethylenebisacetamide-induced erythroid differentiation of the cells. This protein is tightly bound to the chromatin and does not appear to be related to any of the known histones. The protein was not induced in a dimethyl sulfoxide-resistant variant of these cells, indicating that its presence is associated with erythroid differentiation. (33 refs.)

77-4766 **In Vitro Protein Synthesizing Activity of Rat Liver as Influenced by a Physiological Dose of Cortisone and Dibutyryl Cyclic AMP.** (Eng.) Hoshino, J. (Robert Koch Institut, 1000 Berlin 65, W. Germany) Kuhne, U.; Studinger, G.; Kroger, H. *Biochem Biophys Res Commun* 74(2): 663-669; 1977.

The cell-free protein-synthesizing activity of isolated total liver polysomes was reduced by the administration of a low dose of cortisone acetate in adrenalectomized female Wistar rats. Dibutyryl cyclic AMP also inhibited this activity, but its effect is due to inactivation of the soluble fraction. A combination of both drugs yielded polysomes that were twice as active as those of untreated controls. (14 refs.)

77-4767 **A New Method for Sequencing DNA.** (Eng.) Maxam, A. M. (Dept. Biochemistry and Molecular Biology, Harvard Univ., Cambridge, MA 02138) Gilbert, W. *Proc Natl Acad Sci USA* 74(2): 560-564; 1977.

DNA can be sequenced by a chemical procedure that partially breaks a terminally labeled DNA molecule at each repetition of a base. The lengths of the labeled fragments then identify the positions of that base. Reactions are described that cleave DNA preferentially at guanines, at adenines, at cytosines and thymines equally, and at cytosines alone. When the products of these four reactions are resolved by size, using electrophoresis on a polyacrylamide gel, the DNA sequence can be read from the pattern of radioactive bands. The technique will permit sequencing of at least 100 bases from the point of labeling. (13 refs.)

77-4768 **Purified DNAs are Transcribed after Microinjection into *Xenopus* oocytes.** (Eng.) Mertz, J. E. (Medical Res. Council Lab. Molecular Biology, Hills Rd., Cambridge CB2 2QH, England); Gurdon, J. B. *Proc Natl Acad Sci USA* 74(4): 1502-1506; 1977.

Experimental data is presented demonstrating that RNA transcripts are synthesized for at least 5 days from purified DNAs of simian virus 40 microinjected into eggs or germinal vesicles of oocytes from *Xenopus laevis.* The quantity of virus-specific RNA produced was roughly proportional to the amount of DNA injected. (28 refs.)

77-4769 **Cyclic Variation of DNA Synthesis in Human Breast Epithelium.** (Eng.) Masters, J. R. (Dept. Pathology, St. Paul's Hosp., Inst. Urology, 24 Endell St., London, WC2H 9AE, England); Drife, J. O.; Scarisbrick, J. J. *J Natl Cancer Inst* 58(5): 1263-1265; 1977.

Autoradiography was used to examine DNA synthesis in normal breast epithelium from 47 premenopausal women. In parous women, the labeling index decreased during the follicular phase of the menstrual cycle and increased to a significantly higher level during the luteal phase. Cyclic variation was not demonstrated in the nulliparous group. (8 refs.)

77-4770 **Rat Mammary Deoxyribonucleic Acid Synthesis During the Estrous Cycle, Pregnancy, and Lactation in Relation to Mammary Tumorigenesis. Its Implication for Human Breast Cancer.** (Eng.) Nagasawa, H. (Pharmacology Div., Natl. Cancer Center Res. Inst., Tsukiji 5-1-1, Chuo-ku, Tokyo 104, Japan) Vorherr, H. *Am J Obstet Gynecol* 127(6): 590-593; 1977.

Measurements of mammary DNA synthesis in Sprague-Dawley rats showed a peak activity on the afternoon of estrus, followed by a decrease during the remainder of the cycle. Synthesis during pregnancy peaked on day 6 and abruptly decreased thereafter, remaining low throughout lactation. Pregnancy and lactation may therefore have protective effects against mammary tumorigenesis. (35 refs.)

77-4771 **The Sequence Specificity of Vertebrate DNA Methylation.** (Eng.) Browne, M. J. (Dept. Biochemistry, Glasgow Univ., Glasgow G12 8QQ, Scotland) Burdon, R. H. *Nucleic Acids Res* 4(4): 1025-1037; 1977.

The relative quantity of 5-methylcytosine in vertebrate nuclear DNA shows species and tissue variation. To determine whether this is due to the action of species- or cell-specific DNA methylases, the sequence specificity of 5-methylcytosine was studied in DNA from polyoma virus-transformed and normal baby hamster kidney cells, mouse L929 cells, a simian virus 40-transformed mouse cell line, HeLa cells, Chang liver cells, and a *Xenopus laevis* liver cell line. The pattern of methylation was remarkably constant, indicating stringent evolutionary conservation of vertebrate DNA methylation. (40 refs.)

77-4772 **Effect of Cycloheximide on the Synthesis and Processing of 5S RNA in HeLa Cells.** (Eng.) Hayashi, Y. (Dept. Biochemistry, Tokushima Univ. Sch. Medicine, Tokushima 770, Japan) Kominami, R.; Muramatsu, M. *J Biochem (Tokyo)* 81(2): 451-459; 1977.

The inhibitory effects of cycloheximide (CH) on the synthesis of 5S protein in HeLa cells were examined. The synthesis of 5S RNA was inhibited by 25%-30% within 1 hr of the addition of 100 μg/ml CH, the degree of inhibition thereafter remaining constant. The extent and kinetics of this inhibition were different from those of the inhibition of high-molecular-wt RNA, suggesting that its synthesis is not directly regulated by the short-lived protein implicated in 45S RNA synthesis. CH inhibited the appearance of newly synthesized 5S RNA in cytoplasmic ribosomes by >60%, presumably reflecting the inhibition of 60S ribosomal subunit formation. CH also appeared to inhibit selectively the appearance of 18S RNA in the cytoplasm. (25 refs.)

77-4773 **RNA Transport in Isolated Myeloma Nuclei. Transport from Membrane-denuded Nuclei.** (Eng.) Stuart, S. E. (Dept. Biochemistry, Michigan State Univ., East Lansing, MI 48824); Clawson, G. A.; Rottman, F. M.; Patterson, R. J. *J Cell Biol* 72(1): 57-66; 1977.

After removal of nearly 90% of the nuclear phospholipid by detergent treatment, the membrane-denuded nuclei of MOPC-21 mouse myeloma cells remained intact. RNA transport continued unchanged and was not affected by temperature. It was concluded that the transport of macromolecules from isolated myeloma nuclei is independent of the nuclear membrane. (25 refs.)

77-4774 **Poly (A)-binding RNAs from Nuclei and Polysomes of BHK-21 Cells.** (Eng.) Burdon, R. H. (Dept. Biochemistry, Univ. Glasgow, Glasgow G12 8QQ, Scotland); Shenkin, A.; Douglas, J. T.; Smillie, E. J. *Biochim Biophys Acta* 474(2): 254-267; 1977.

Using either a Millipore-poly(A)-binding assay or columns of poly (A)-Sepharose 4B, the presence of an RNA species with high affinity for poly(A) was detected in the nuclei and cytoplasm of cultured BHK-21/C13 cells. A class of messenger RNA's lacking poly(A) was also observed in HeLa cells. The nuclear species labels rapidly, is metabolically unstable, and appears to be a specific subclass of heterogenous nuclear RNA. (33 refs.)

77-4775 **The Effect of Tryptophan on Nucleocytoplasmic Translocation of RNA in Rat Liver.** (Eng.) Murty, C. N. (Dept. Pathology, Univ. South Florida, Coll. Medicine, Tampa, FL 33620); Verney, E.; Sidransky, H. *Biochim Biophys Acta* 474(1): 117-128; 1977.

When tryptophan was given to fasted female Sprague-Dawley rats pretreated with cordycepin and actinomycin D, there was a decreased level of nuclear poly (A)-messenger RNA (mRNA) and a concomitant increased level of cytoplasmic polyribosomal poly (A)-mRNA in the liver. These results suggest that in the rat, tryptophan increases the rate of translocation of hepatic poly (A)-mRNA from the nucleus to the cytoplasm. (28 refs.)

77-4776 **Metabolic Characteristics of Messenger RNA in Tumor Cells and Tissues of the Host Organism.** (Rus.) Shapot, V. S. (Oncological Scientific Center, Acad. Medical Sciences USSR, Moscow, USSR) Alekhina, R. P.; Zaboikin, M. M.; Likhtenshtein, A. V. *Vestn Akad Med Nauk SSSR* (3): 64-69; 1977.

The systemic effect of a tumor on a host organism was studied in random-bred albino rats and in Wistar rats with transplanted Zaidel hepatoma. Animals were given actinomycin D (A-D: 1-1.5 mg/rat) and, 1 hr later, they were injected with ^{3}H- or ^{14}C- orotic acid [to label liver messenger RNA (mRNA)] and with ^{3}H- or ^{14}C-thymidine (to label hepatoma mRNA). The nuclear and cytoplasmic mRNA in the livers of control and tumor-bearing rats and in the hepatomas was assessed by ion-exchange chromatography. The radioactivity of the nuclear RNA decreased fastest in the hepatoma cells. Two hours after the A-D-induced block of RNA synthesis, the radioactivity in the hepatoma cells was 45%-54% of the initial level, compared to 55%-68% in the liver of tumor-bearing rats and to 70%-74% in the liver of control animals. A fraction of rapidly labeling cytoplasmic mRNA was observed in the hepatoma and in the liver of tumor-bearing animals, but this fraction was absent in the controls. (12 refs.)

77-4777 **Hormonal Control of Transcription in the Rat Uterus. Stimulation of Deoxyribonucleic Acid-dependent RNA Polymerase III by Estradiol.** (Eng.) Weil, P. A. (Dept. Biological Chemistry, Washington Univ., St. Louis, MO 63110) Sidikaro, J.; Stancel, F. M.; Blatti, S. P. *J Biol Chem* 252(3): 1092-1098; 1977.

Uteri from mature rats, immature rats, and estrogen-treated immature rats contain two forms of RNA polymerase II, IIA and IIIB. These enzymes could be distinguished from uterine RNA polymerases I and II on the basis of elution from DEAE-Sephadex columns and on the basis of sensitivity to α-amanitin. (40 refs.)

77-4778 **RNA Polymerase-Promotor Complex Stability on Supercoiled and Relaxed DNA.** (Eng.) Warner, C. K. (Dept. Biology, Emory Univ., Atlanta, GA 30322) Schaller, H. *FEBS Lett* 74(2): 215-219; 1977.

To investigate why RNA polymerase transcribes superhelical DNA more efficiently than relaxed DNA, the stability of the polymerase/promotor region complex was measured on superhelical and relaxed simian virus 40 (SV40) DNA. RNA polymerase was from *Escherichia coli.* Under the conditions used (high salt, low temperature), the polymerase/promotor complex was much more stable in superhelical than in relaxed DNA. At 240 mM KCl and O C, the superhelical DNA/polymerase complex dissociated with a half-life of 210 min, compared to a half-life of 2 min for the relaxed DNA/ polymerase complex. The results are consistent with the hypothesis that promotor complex formation requires local unwinding of base pairs in the promotor region DNA, which is energetically favored in the superhelical form. (20 refs.)

77-4779 **Action of Pancreatic DNase: Requirements for Activation of DNA as a Template-Primer for DNA Polymerase α.** (Eng.) Baril, E. (Worcester Foundation Experimental Biology, Incorporated, Shrewsbury, MA 01545) Mitchener, J.; Lee, L.; Baril, B. *Nucleic Acids Res* 4(8): 2641-2653; 1977.

$Ca^{2}+$ and $Mg^{2}+$ are essential for the preparation by pancreatic DNase of activated DNA as a template-primer for DNA polymerase α. $Ca^{2}+$ and $Mg^{2}+$ are also required for the production of a hyperchromic shift by DNase; under these conditions the enzyme produces double-strand scissions in the DNA. (12 refs.)

77-4780 **Inactivation of Avian Myeloblastosis Virus DNA Polymerase by Specific Binding of Pyridoxal 5′-Phosphate to Deoxynucleoside Triphosphate Binding Site.** (Eng.) Papas, T. S. (Lab. Tumor Virus Genetics, NCI, Bethesda, MD 20014) Pry, T. W.; Marciani, D. J. *J Biol Chem* 252(4): 1425-1430; 1977.

Deoxynucleoside 5′-triphosphate (dTTP) protected avian myeloblastosis virus DNA polymerase from inactivation by pyridoxal 5′- phosphate. Reduction of the pyridoxal 5′-phosphate enzyme complex in the presence or absence of dTTP showed that the α subunit possesses five reactive amino groups, one of which is essential for catalytic activity; the β subunit has three reactive amino groups not involved in the deoxynucleoside binding site. (32 refs.)

77-4781 **Triiodothyronine Stimulates Specifically Growth Hormone mRNA in Rat Pituitary Tumor Cells.** (Eng.) Seo, H. (Thyroid Study Unit, Univ. Chicago, Sch. Medicine, Chicago, IL 60637) Vassart, G.; Brocas, H.; Refetoff, S. *Proc Natl Acad Sci USA* 74(5): 2054-2058; 1977.

The effect of thyroid hormone on the synthesis and messenger RNA (mRNA) activity of growth hormone (GH) in rat pituitary cells grown in culture was investigated. Translation was carried out in a rabbit reticulocyte lysate cell-free system, and GH and prolactin synthesis in the lysate was measured by double antibody precipitation. In the lysate, total RNA extracted from rat pituitary tumor cells directed, in a dose-related manner, the synthesis of proteins that were precipitated by antisera specific to rat growth hormone (somatotropin) and rat prolactin. There was a decrease in GH secretion and GH mRNA activity when the cells were grown in a medium deficient in thyroid hormone. Addition of triiodothyronine in physiologic amounts both prevented and completely reversed this effect within 48 hr. Thyroid hormone had no effect on prolactin secretion or prolactin mRNA activity. These results suggest that thyroid hormone may stimulate the synthesis of GH through induction of transcriptional activity. (29 refs.)

77-4782 **T.S.H. Receptor and Adenylate Cyclase in Undifferentiated Thyroid Carcinoma (Letter to Editor).** (Eng.) Abe, Y. (Dept. Medicine, Keio Univ., Tokyo, Japan) Ichikawa, Y.; Homma, M.; Ito, K.; Mimura, T. *Lancet* 2(8036): 506; 1977.

Studies with human thyroid carcinomas indicated that differentiated carcinomas are under the influence of thyroid stimulating hormone (TSH), have a receptor for the hormone, and have a TSH-sensitive adenylate cyclase. This was not true of undifferentiated thyroid carcinomas. (6 refs.)

77-4783 **Somatostatin-Immunoreactive Cells in Medullary Carcinoma of the Thyroid.** (Eng.) Sundler, F. (Histologiska Institutionen, Biskopsgatan 5, S-223 62 Lund, Sweden) Alumets, J.; Hakanson, R.; Bjorklund, L.; Ljungberg, O. *Am J Pathol* 88(2): 381-386; 1977.

Immunohistochemical studies of 10 medullary carcinomas of the thyroid were performed using antisera against calcitonin, somatostatin, and ACTH. In addition to calcitonin cells, eight of the tumors contained varying numbers of somatostatin-immunoreactive cells. No ACTH-immunoreactive cells were found. The results indicate that thyroid medullary carcinomas are often multihormonal and that somatostatin is common in these tumors. Unlike calcitonin cells, somatostatin cells are not found in normal human thyroid tissue. (21 refs.)

77-4784 **In Vitro Hormone Response of Beagle Mammary Dysplasias (Meeting Abstract).** (Eng.) Warner, M. R. (Anatomy Dept., Univ. California, Davis, CA 95616) *Proc Am Assoc Cancer Res* 18: 1; 1977. (no refs.)

77-4785 **Tumor-Inhibition By Deoxycorticosterone (DOC) and Enhancement by Cortisone (Meeting Abstract).** (Eng.) Padawer, J. (Albert Einstein Coll. Medicine, New York, NY 10461) Rettura, G.; Seifter, E. *Proc Am Assoc Cancer Res* 18: 28; 1977. (no refs.)

77-4786 **Cell-Surface Glycosyltransferases in Cultured Fibroblasts: Increased Activity and Release During Serum Stimulation of Growth.** (Eng.) LaMont, J. T. (Div. Gastroenterology, Peter Bent Brigham Hosp., Boston, MA 02115) Gammon, M. T.; Isselbacher, K. J. *Proc Natl Acad Sci USA* 74(3): 1086-1090; 1977.

The relationship between cell-surface galactosyltransferase (GT) and cell division was explored in serum-stimulated NIL and BHK/C13 strains of baby hamster kidney fibroblasts and their polyoma virus-transformed counterparts. The cell-surface location of GT was demonstrated in experiments with the enzyme modifier α-lactalbumin, the addition of which to the assay medium for GT resulted in accumulation of lactose in the medium but not in the cells. This would not occur if the enzyme catalyzing this reaction were intracellular, because α-lactalbumin does not enter the cell and, therefore, does not alter substrate specificity. There was no detectable hydrolysis of UDP-galactose to free galactose by the BHK fibroblasts, nor did a hundredfold molar excess of free galactose inhibit cell-surface GT. There was a marked increase in specific activity of cell-surface exogenous GT in serum-stimulated fibroblasts compared to resting fibroblasts. Dividing (but not resting) fibroblasts released GT, but not sialyltransferase or fucosyltransferase, in soluble form into the tissue culture medium. The release of GT was greater from virally transformed than from nontransformed fibroblasts. This increase release of GT in transformed cells may reflect accelerated membrane turnover or remodeling of surface membranes in these cells. (28 refs.)

77-4787 **The Relationship Between Surface Protease Activity and the Rate of Cell Proliferation in Normal and Transformed Cells.** (Eng.) Hatcher, V. B. (Dept. Biochemistry, Albert Einstein Coll. Medicine, Montefiore Hosp. and Medical Center, Bronx, NY 10467); Oberman, M. S.; Wertheim, M. S.; Rhee, C. Y.; Tsein, G.; Burk, P. G. *Biochem Biophys Res Commun* 76(2): 602-608; 1977.

Surface protease activity was investigated in growth-inhibited normal rabbit aortic fibroblasts and smooth muscle cells and in transformed human melanoma (HM-34) cells and mouse epidermal (UT-1) cells that were not growth-inhibited. A decrease in activity was seen at high cell density, when replication ceased only in the normal aortic cells. The decrease was related to a decrease in cell proliferation. (23 refs.)

77-4788 **Protease Effects on Specific Growth Properties of Normal and Transformed Baby Hamster Kid-**

ney Cells. (Eng.) Brown, M. (Dept. Microbiology and Immunology, Univ. Washington, Seattle, WA 98195) Kiehn, D. *Proc Natl Acad Sci USA* 74(7): 2874-2878; 1977.

The effects of exogenous protease (trypsin, pronase, and plasmin) on the growth of normal baby hamster kidney cells (BHK) and polyoma virus-transformed cells (Py BHK) were examined using the classical culture assays for transformation. The primary effect of the three proteases was to lower the serum requirement. The effect of viral transformation on the serum requirement of BHK cells was about 10 times greater than the max effect of the proteases. Proteases did not affect the max saturation density or the plating efficiency in soft agar of either BHK or Py BHK. Under conditions optimal for growth stimulation, protease decreased the strength of cell-to-substrate adhesion but did not affect cellular morphology. In contrast to previous studies, experiments using highly purified trypsin and several different active-site inhibitors suggest that the growth-stimulatory activity of trypsin is not directly related to the proteolytic activity of the molecule. An alternative to the possibility of a dissociation of growth-stimulatory activity from proteolytic activity on the trypsin molecule is that mitogenic activity might reside in tryptic fragments or peptides in the trypsin preparations. (69 refs.)

77-4789 **Inhibition of Initiation by the Protease Inhibitors, Antipain and Leupeptin (Meeting Abstract).** (Eng.) Belman, S. (Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY 10016) Rossman, T.; Troll, W. *Proc Am Assoc Cancer Res* 18: 32; 1977. (no refs.)

77-4790 **Histaminase (Diamine Oxidase) Activity in Human Tumors: An Expression of a Mature Genome.** (Eng.) Baylin, S. B. (Room 806, Traylor Building., Johns Hopkins Sch. Medicine, 720 Rutland Ave., Baltimore, Md 21205) *Proc Natl Acad Sci USA* 74(3): 883-887; 1977.

The type of gene responsible for histaminase activity in human tumors and placenta was examined, and histaminases from different normal tissues were compared. The electrophoretic mobility and Km for the deamination of histamine and putrescine were identical for histaminases from human placenta and from medullary thyroid carcinoma. An antibody prepared to highly purified human placental histaminase was used to examine the cross reactivity of histaminase from normal and neoplastic human tissues and tissues from rat and pig. Identical patterns of immunoreactivity were found for histaminase from human placenta, kidney, medullary thyroid carcinoma, and small cell lung carcinoma. Human intestinal histaminase cross reacted well but less strongly than did enzymes from these other tissues. Histaminases from pig kidney, pig intestine, and rat intestine showed no cross reaction; histaminase from rat thymus and adrenal gland showed minimal cross reactivity. Histaminase activity in placental and tumor tissues appears to be the expression of a mature genome and not a unique expression of fetal tissues. This finding is consistent with earlier suggestions that placental histaminase is associated not with trophoblastic tissue but with maternal decidual elements in placenta. These findings also indicate that histaminase activity could be a property of normal tissues from which certain tumors arise. (30 refs.)

77-4791 **Characterization of Pyrimidine Nucleoside Monophosphokinase in Normal and Malignant Tissues.** (Eng.) Arima, T. (Dept. Enzyme Physiology, Inst. Enzyme Res., Sch. Medicine, Tokushima Univ., Tokushima 770, Japan) Akiyoshi, H.; Fujii, S. *Cancer Res* 37(6): 1593-1597; 1977.

Nucleoside monophosphokinase was purified from Yoshida sarcoma and normal rat liver (male albino Wistar-King and male Donryu rats), and its specificity for phosphate acceptors and the kinetics of substrate utilization and inhibition were investigated. Phosphorylation of deoxyuridine 5′-monophosphate (dUMP) was catalyzed by deoxythymidine 5′-monophosphate (dTMP) kinase and by deoxycytidine 5-monophosphate (dCMP) kinase. The activity of dCMP kinase for dUMP phosphorylation was indicated by the results of hydroxylapatite column chromatography, in which the dUTP phosphatase was completely separated from dCMP kinase, resulting in dUMP phosphorylation. The evidence that dCMP kinase is identical to dUMP kinase was also confirmed by the finding that dCMP competitively inhibited the phosphorylation of dUMP and vice versa and that the reciprocal relationship of the enzyme activity of dUMP kinase in Yoshida sarcoma and in normal rat liver is the same as that of dCMP kinase. It is concluded that there are two species of pyrimidine nucleoside monophosphokinase, the larger one (molecular wt 46,000) catalyzing phosphorylation of dTMP and dUMP and the smaller one (molecular wt 26,000) catalyzing phosphorylation of UMP, dCMP, CMP, and dUMP. Resting cells contain only the latter enzyme, but in proliferating cells dTMP-dUMP kinase is induced. In the latter cells, dUTP phosphatase that specifically masks dUMP kinase is induced concomitantly, facilitating the supply of necessary nucleotides for DNA synthesis. (13 refs.)

77-4792 **Subunit Interaction in Cyclic AMP-dependent Protein Kinase of Mutant Lymphoma Cells.** (Eng.) Hochman, J. (Dept. Zoology, Hebrew Univ. Jerusalem, Israel) Bourne, H. R.; Coffino, P.; Insel, P. A.; Krasny, L.; Melmon, K. L. *Proc Natl Acad Sci USA* 74(3): 1167-1171; 1977.

The interaction of the regulatory (R) and catalytic (C) subunits of cyclic AMP (cAMP)-dependent protein kinases derived from normal or wild-type (WT) mouse S49 lymphoma cells and from mutant S49 cells expressing kinase activity with altered affinity for cAMP was examined. Subunit recombination experiments were performed using purified WT and mutant R subunits and C subunits purified from WT cells. Compared to WT R subunits, only one-sixth as much mutant R subunit was required to reassociate with and suppress 50% of C-subunit activity at equilibrium. Sodium thiocyanate activated cAMP-dependent kinase of both cell types by causing the holoenzyme to dissociate. In comparison with WT , a two-fold higher concentration of sodium thiocyanate was required to maximally activate the kinase in mutant extracts. Both the reassociation result and the increased resistance of the mutant enzyme to a nonspecific dissociating agent (the thiocyanate) suggest that the mutant R subunit binds C subunit more tightly than does the WT R subunit. This interpretation raises the possibility that increased R-C subunit binding affinity in the mutant cell is responsible for the increased apparent affinity constant for activation by cAMP of the mutant holoenzyme and, therefore, for the decreased potency of cAMP in regulating intact mutant cells. (17 refs.)

77-4793 **Partial Purification, Properties and Regulation of Inosine 5′-Phosphate Dehydrogenase in Normal and Malignant Rat Tissues.** (Eng.) Jackson, R. C. (Lab. Experimental Oncology, Indiana Univ. Sch. Medicine, Indianapolis, IN 46202) Morris, H. P.; Weber, G. *Biochem J* 166(1): 1-10; 1977.

The partial purification, properties, and comparative studies of inosine 5′-phosphate dehydrogenase (IMP) in developing and regenerating liver and in transplantable hepatomas and kidney tumors are reported. IMP dehydrogenase was purified 180-fold from rat liver and from the transplantable rat hepatoma 3924A. The enzymes from the two sources appeared to be identical in every respect examined, kinetic properties, pH optimum, and susceptibility to inhibitors. There was no indication that malignant transformation altered enzyme properties. IMP dehydrogenase activity was increased in a series of rat hepatomas compared to normal liver by 2.5-13 times; these increases correlated with tumor growth rate. Activity in two rat kidney tumors was increased three times over normal renal cortex. Eighteen hours after partial hepatectomy in rats, IMP dehydrogenase activity reached a peak of 580% of normal. In neonatal liver, however, activity was only slightly higher than in the normal adult liver. In livers of rats starved for 3 days, in which all enzymes except those involved in gluconeogenesis showed decreased activity, IMP dehydrogenase activity was increased; this increase was accompanied by a rise in hepatic guanosine triphosphate (GTP) activity. It is concluded that IMP dehydrogenase is the key enzyme in the regulation of GTP production and thus biosynthesis, that the activity shows a correlation with cell proliferation in both normal and malignant cell populations, and that the disproportionate increase found in malignant cells of rat liver and kidney may be linked with neoplastic transformation. (38 refs.)

77-4794 **Synthesis and Activation of Mitotic Ca^{2}+-Adenosinetriphosphatase During the Cell Cycle of Mouse Mastocytoma Cells.** (Eng.) Petzelt, C. (Inst. Cell Res., German Cancer Res. Center, P. O. Box 101949, D-6900 Heidelberg, W. Germany); Auel, D. *Proc Natl Acad Sci USA* 74(4): 1610-1613; 1977.

The synthesis and activity of mitotic Ca^{2}+- ATPase were measured through the entire cell cycle in a total of 4 × 10^7 (2 × 10^5/ml) synchronized mouse mastocytoma P-815X2 cells. Determination of enzymatic activity every 2 hr for a total of 16 hr showed a rise in activity whenever the mitotic phase was reached. The rate of ^{14}C-labeled amino acid incorporation into the enzyme fraction during the cell cycle indicated that the enzyme is activated at mitosis. A distinct max of enzyme synthesis occurred during interphase, which occurs at the beginning of the S phase. Ca^{2}+-ATPase and/or other factors may activate constituent of the mitotic apparatus to allow formation of the mitotic spindle. (42 refs.)

77-4795 **Localization of the Catalytic Site of 5′-Nucleotidase at the Inner Surface of Murine Plasmocytoma Plasma Membranes.** (Eng.) Zachowski, A. (Station de Recherches de Virologie et d'Immunologie INRA, Route de Thiverval, 78850 Thiverval-Grignon, France) Aubry, J.; Jonkman-Bark, G.; Lelievre, L. *FEBS Lett* 75(1): 197-200; 1977.

To determine the position of the catalytic site of 5′-nucleotidase, the activity of this enzyme was tested with intact and disrupted MF_2S cells derived from an MOPC murine plasmocytoma. With intact cells, only the outer face of the membrane interacts with the substrate; with disrupted cells, the substrate is exposed to catalytic sites on both sides of the membrane. Comparisons were made with (Na+/K+)-ATPase, whose catalytic site is known to be located at the inner face of the membrane. Intact cells were suspended at 37 C in 0.16 NaCl or in Eagle's medium, and cell death and enzyme activity were determined at various times. Enhancement of specific activity in these cells paralleled the cell-surface permeability (due to 40 mM imidazole or 0.1% DOC added to the medium). No alkaline phosphatase (AP) was found. Disrupted cells were formed after incubation in lytic medium, and the percentage of broken cells and enzyme activity were determined. The specific activity increased with time as cell breakage increased. The behavior of 5′-nucleotidase closely paralleled that of (Na+/K+)-ATPase. Again, no AP activity was found. Experiments with inside-out and right-side-out plasma membrane vesicles showed that 5′-nucleotidase specific activity is about three times higher in the inside-out vesicles. It is concluded that the 5′-nucleotidase catalytic site is located at the inner face of the murine plasmocytoma plasma membrane. (20 refs.)

7-4796 **Purine Metabolic Cycle in Normal and Leukemic Leukocytes.** (Eng.) Dietz, A. A. (Res. Service, Veterans Admin. Hosp., Hines, IL 60141) Czebotar, V. *Cancer Res* 37(2): 419-426; 1977.

The complete purine metabolic cycle was studied in 300 million WBC from four normal persons and nine patients with chronic lymphocytic leukemia (CLL). Fifteen enzymes involved in purine metabolism were surveyed. Quantitation is given in terms of enzyme activity per milligram of protein in the extract per minute of incubation, or per 10^{10} cells/min. Extraction of 350,000 normal lymphocytes/μl gave a soluble protein concentration of 1.46 mg/ml, but the yield from the same number of CLL lymphocytes varied from 0.72 to 8.32 mg/ml. Normal and leukemic cells showed little difference in purine nucleoside phosphorylase, purine phosphoribosyltransferase, and inosine monophosphate dehydrogenase activities. However, 5′-nucleotidase activity was greater in CLL cells than in normal cells. This activity was inversely correlated with the concentration of extractable protein. In individual cases of CLL, the protein concentrations and 5′-nucleotidase activities extended below and above the normal values. In most cases, the adenosine deaminase activity of CLL cells was lower than normal, that of adenosine kinase higher than normal. In CLL cells, these two enzymes gave a positive correlation with one another. In addition, the adenylate and guanylate kinase activities were much higher in CLL cells than in normal cells. (40 refs.)

77-4797 **Differences Between Rat Liver Epithelial and Fibroblast Cells in Sensitivity to 8-Azaguanine and Metabolism of Purines (Meeting Abstract).** (Eng) Berman, J. J. (Naylor-Dana Inst., Valhalla, NY 10595); Tong, C.; Williams, G. M. *In Vitro* 13(3): 196; 1977. (no refs.)

77-4798 **Effect of High-Risk Diets for Colon Carcinogenesis on Intestinal Mucosal and Bacterial β-Glucuronidase Activity in F344 Rats.** (Eng) Reddy, B. S. (Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY 10595); Mangat, S.; Weisburger, J. H.; Wynder, E. L. *Cancer Res* 37(10): 3533-3536; 1977.

The effect of high-protein (beef or soybean protein) and high-fat (beef fat, corn oil, or lard) diets on large intestinal bacterial and intestinal mucosa β-glucuronidase (GUD) was studied in female F344 rats maintained on these diets for two generations. Animals fed a 20% corn oil or 20% lard and 20% casein diet had a higher GUD activity in the contents of the cecum and colon than did rats fed a 5% corn oil or lard and 20% casein diet. The cecal bacterial GUD activity was higher in animals fed diets with high levels of beef protein (40%) and beef fat (23%) or with high levels of soybean protein (39%) and corn oil (24%) than it was in rats fed diets containing 18.5% beef protein and 6.5% beef fat or 19% soybean protein and 5.4% corn oil. Animals fed diets containing high levels of beef protein and fat or high levels of soybean protein and corn oil had a higher small intestinal mucosal GUD activity than did the other groups. No significant difference was observed in the colonic mucosal GUD activity among the animals fed beef and soybean diets. It is concluded that diets high in fat and high or normal in protein are associated with elevated levels of bacterial GUD activity in the rat large intestine. (25 refs.)

77-4799 **Trends in the Study of the Role of Nutritional Factors in the Development of Malignant Neoplasms.** (Rus) Martynenko, A. M. (Dept. Oncology, Central Oncological Hosp., Shatura, USSR). *Vopr Onkol* 23(9): 70-74; 1977.

The effect of a dietary regimen on 449 patients with precancerous lesions, 192 patients with malignancies receiving radio- and chemotherapy, and 398 patients prior to and after radical cancer surgery was investigated. The diet contributed to a decrease in the incidence of precancerous lesions and a reduction in their tendency toward malignant transformation, increased glycolysis and tissue respiration, lowered levels of lactic acid and cholesterol in the blood, reduced the degree of malignancy, increased periods of remission, and reduced the incidence of tumor recurrence. (12 refs.)

77-4800 **Respiratory Characteristics of Mitochondria Isolated from Squamous Epithelium of the Hamster Cheek Pouch.** (Eng) McCoy, G. D. (Div. Molecular Biology and Pharmacology, Naylor Dana Inst. for Disease Prevention, Valhalla, NY 10595). *Proc Soc Exp Biol Med* 156(1): 118-122; 1977.

A method is presented for the preparation of epithelial sheets from the cheek pouches of Syrian golden hamsters. An analysis of respiration as compared to liver mitochondria revealed that squamous epithelial mitochondria have increased rotenone-insensitive NADH cytochrome c reductase activity; succinate cytochrome c reductase, oligomycin sensitive ATPase, and cytochrome oxidase activities were decreased. The ratios of cytochromes c/a + a_3 and b/a + a_3 were lower in squamous epithelial mitochondria. This type of biochemical investigation of tissue-specific effects could be useful in understanding the etiology of diet-related cancers. (17 refs.)

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ABBREVIATIONS

JOURNAL names are abbreviated according to the *List of Journals Indexed in Index Medicus, Abbreviation Listing*. If the journal is not listed in this, abbreviations are derived from the *International List of Periodical Title Word Abbreviations*.

LANGUAGE of the article is indicated in parentheses after the title and is represented by a three-letter code. The source for these codes is *MARC Manuals Used by the Library of Congress*, pages 183-187.

ABBREVIATIONS used in abstracts:

A	angstrom(s)
ACTH	adrenocorticotropic hormone
ADP	adenosine diphosphate
AMP	adenosine monophosphate
ATP	adenosine triphosphate
approx	approximately
av	average
BCG	bacillus Calmette-Guerin
bid	twice daily
C	degree(s) centigrade
cal	calorie(s)
kcal	kilocalorie(s)
cc	cubic centimeter(s)
Ci	curie(s)
mCi	millicurie(s)
μCi	microcurie(s)
cm	centimeter(s)
CNS	central nervous system
cpm	counts per minute
DNA	deoxyribonucleic acid
ED$_{50}$	median effective dose
EDTA	ethylenediamine tetraacetic acid
g	gram(s)
kg	kilogram(s)
mg	milligram(s)
μg	microgram(s)
Hb	hemoglobin
hr	hour(s)
ia	intra-arterial
id	intradermal
IgA	Immunoglobulin A
IgB	Immunoglobulin B
IgG	Immunoglobulin G
IgM	Immunoglobulin M
ILS	increased life span
im	intramuscular
ip	intraperitoneal
IU	International Unit(s)
iv	intravenous
Km	Michaelis constant
LD	lethal dose
LD$_{50}$	median lethal dose
M	molar
μM	micromolar
mOsm	milliosmolar
max	maximum
mEq	milliequivalent(s)
min	minute(s)
ml	milliliter(s)
μl	microliter(s)
mm	millimeter(s)
mo	month(s)
mol wt	molecular weight
N	normal concentration
NAD	nicotinamide adenine dinucleotide
NADH	reduced nicotinamide adenine dinucleotide
NADP	nicotinamide adenine dinucleotidephosphate
NADPH	reduced nicotinamide adenine dinucleotidephosphate
NCI	National Cancer Institute
NIH	National Institutes of Health
PAS	periodic acid-Schiff
po	orally
ppb	parts per billion
ppm	parts per million
qid	four times daily
qod	every other day
QO$_2$	oxygen quotient
R	roentgen
RBC	red blood cells (erythrocytes)
RNA	ribonucleic acid
rpm	revolutions per minute
sc	subcutaneous
sec	second(s)
SGOT	serum glutamic-oxaloacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
soln	solution
TCD	tissue culture dose
TCD$_{50}$	median tissue culture dose
tid	three times daily
UV	ultraviolet
WBC	white blood cells (leukocytes)
wk	week(s)
wt	weight
X	times
yr	year(s)

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REVIEW

7-4801 **Cancer and Chemicals.** (Eng) Corbett, T. H. (Chicago: Nelson-Hall): 210 pp.; 1977.

t is estimated that over 80% of all cancers are caused by nvironmental pollutants. The widespread prevalence of hese chemicals in occupational settings, food, consumer prolucts, water, domestic situations, and medical settings is disussed. It is suggested that it is already too late to prevent ancer in many persons who have already been exposed to arcinogens; but if safeguards are not enforced and thorough esting done, cancer will continue to increase in incidence. ome methods of minimizing exposure are listed. Some of the arcinogens considered are polyvinyl chloride, styrene oxide, rethane, diethylstilbestrol, methylcholanthrene, asbestos nd benzene. (no refs.)

77-4802 **Simple Theoretical Criterion of Chemical Carcinogenicity.** (Eng) Veljkovic, V. (Lab. Theoretical Physics, Boris Kidric Inst., 11001 Belgrade, Yugoslavia); Lalovic, D. I. *Experientia* 33(9): 1228-1229; 1977.

The use of the av quasi-valence number (defined as the ratio of the sum of all atomic valence electrons to the number of atoms in the given molecules) for the determination of the carcinogenicity of a given compound is explained. These calculations use the molecular formula of a compound and are not affected by isomerism or primary metabolic alterations; the latter fact explains some of the errors obtained. With this formula, compounds having an av quasi-valence number greater than 3.20 are not carcinogenic, while those having a lesser value are potential carcinogens. This number in itself is a sufficient index of noncarcinogenicity; for potentially carcinogenic compounds, further indication of carcinogenic activity is needed. This formula can be used for a theoretical prediction of carcinogenic potential. (8 refs.)

77-4803 **The Risk Equations. The Threshold Controversy.** (Eng) Gehring, P. (Toxicology Res., Dow Lab., MI). *New Sci* 75(1065): 426-429; 1977.

The problem of interpreting chemical carcinogen assays in animals is discussed in the context of dose-response curves. A model of the fate of a chemical in the body is presented that can be used to plot dose against nongenetic material bound covalently with a reactive metabolite, genetic material bound covalently with the reactive metabolite and then repaired, and genetic material bound covalently with the metabolite but not repaired. The curves obtained indicate that the amount of reactive metabolite bound to genetic material that escapes repair increases disproportionately as the dose increases. Therefore, data from large-dose animal studies cannot be extrapolated to humans to predict the incidence of cancer following exposure to smaller doses of the same chemical. (1 ref.)

77-4804 **Carcinogenesis: A Late Effect of Irreversible Toxic Damage During Development.** (Eng) Rice, J. M. (Perinatal Carcinogenesis Section, Experimental Pathology Branch, NCI, NIH, Bethesda, MD 20014). *Environ Health Perspec* 18: 133-139; 1976.

The chemical characteristics and biosynthesis of reactive intermediates of transplacental carcinogens, the histologic and biologic features of transplacentally induced tumors, carcinogenesis during early infancy, and in vivo/in vitro bioassy systems are reviewed. In general, intrauterine life and early postnatal life are periods of exceptionally high susceptibility to certain kinds of chemical carcinogens. The most potent of these are the direct-acting alkylating agents. Other known transplacental carcinogens include enzyme-dependent alkylating agents such as dimethylnitrosamine and procarbazine, polynuclear aromatic hydrocarbons, and estrogens. The period of greatest risk occurs in late gestation, usually after organogenesis has begun and after the period of greatest susceptibility to teratogens. Most transplacentally induced tumors in experimental animals have the morphologic features of adult, rather than embryonal tissues, and the types of tumors induced by a given agent tend to be species-specific. The extreme sensitivity of fetal and preweaning rodents and the adaptability of fetal cells to tissue culture facilitate the rapid in vivo/in vitro screening of transplacental chemical carcinogens. (46 refs.)

77-4805 **Genetic Effects of Bisulfite (Sulfur Dioxide).** (Eng.) Shapiro, R. (Dept. Chemistry, New York Univ., New York, NY) *Mutat Res* 39(2): 149-176; 1977.

Studies of the genetic effects of sulfur dioxide are reviewed. The principal sources of exposure to exogenous sulfite are by inhalation of SO_2 in the air and by ingestion of bisulfite in food, beverages, and drugs. In laboratory animals exposed to relatively low levels (which still exceeded by at least 50 times the highest common environmental exposure of the general public), no adverse health effects were observed. At the cellular level, bisulfite can be toxic at concentrations as low as 10^{-2}-10^{-4} M. No lower limit has been established. The effects observed include inhibition of DNA synthesis, cell division, and mitosis accompanied by chromosome abberrations or mutations. This has been demonstrated with microorganisms, plants, and mammalian cells in culture. Epidemiological studies show a clear association between atmospheric SO_2 levels and human respiratory disease. Links of SO_2 to cardiovascular disease and cancer are suggestive, but less firm. In animal experiments a significant cocarcinogenic effect was reported for SO_2 and benzo(a)pyrene. Exposure to SO_2 has also been reported to shorten the induction time for methylcholanthrene carcinogenesis. (138 refs.)

77-4806 **The Genetic Properties of Beta-Propiolactone.** (Eng) Brusick, D. J. (Dept. Genetics, Litton Bionetics, Incorporated, 5516 Nicholson Lane, Kensington, MD 20795). *Mutat Res* 39(3/4): 241-255; 1977.

The toxicity, carcinogenicity, and mutagenicity of β-propiolactone (BPL), the interaction of BPL with macromolecules, the repair of BPL-induced DNA damage; and the results of BPL studies using bacteriophages, bacteria, fungi, drosophila, cultured mammalian cells, and live animals are reviewed. BPL is the most active member of the carcinogenic lactones. Carcinogenicity has been demonstrated in mice, rats, guinea pigs, and hamsters, and sarcomas located at the site of sc injection or skin application are the most common BPL-induced tumors. Since BPL acts directly, requiring no metabolism for activation, there is little species or sex specificity in BPL-induced carcinogenicity. BPL is also extremely active as an initiator in two-step carcinogenesis. It is usually unable to reach systemic organs when administered by typical exposure routes, and most data indicate that the greatest risk to man is the induction of skin cancer. The fact that few organs under hormone influence are target sites for this agent may also be important. (95 refs.)

77-4807 **Mutagenicity of Polycyclic Aromatic Hydrocarbons.** (Eng) Brookes, P. (Chemical Carcinogenesis Div., Inst. Cancer Res., Pollards Wood Res. Station, Nightingales Lane, Chalfont St. Giles, Buckinghamshire HP8 4SP, England). *Mutat Res* 39(3/4): 257-283; 1977.

A review is presented of the genetic hazard to man resulting from polycyclic aromatic hydrocarbons (PAH). The various topics include the structure and metabolism of PAH, their formation and environmental distribution, their carcinogenicity and mutagenicity, their chemical reaction with DNA, and the cytotoxicity and potential for chromosomal damage. It appears that the K-epoxides of the PAH react with the 2-amino groups of guanine in nucleic acids; this could explain the mutagenic and carcinogenic effects of these compounds. It is possible that PAH are connected with colorectal cancer through their generation in vivo by Clostridia, but the association is not clear; associations with cutaneous and breast cancer are also possible. (188 refs.)

77-4808 **Do Aflatoxin and Polycylic Hydrocarbon Carcinogens Delete Genes in the Regions of Chromosomes Acted on by Steroid Hormones?** (Eng) Money-Kyrle, A. F. (39 Gloucester Crescent, London NW1, England). *Med Hypotheses* 3(4): 146-149; 1977.

A hypothesis is presented which can account for some of the changes observed in tumor cells following carcinogenesis by aflatoxin B_1 and polycyclic hydrocarbons. It is proposed that these carcinogens bind to regions of DNA to which steroid hormones bind. The carcinogen then reacts with the guanine bases at these sites; and at cell division, these genes are deleted. This deletion would include genes normally activated or repressed by steroid hormones such as those that bind ribosomes to the endoplasmic reticulum. Thus lysosomal enzymes could be released directly into the cytoplasm and effect changes in contact inhibition, reduce cyclic AMP levels, produce permeability changes, and cause chromosomal abnormalities through DNAses. Experimental evidence supporting this hypothesis is presented, and possible experimental procedures for testing are suggested. (38 refs.)

77-4809 **Smoking and Lung Cancer: More Evidence Needed?** (Swe.) Carlens, E. (No affiliation given). *Lakartidningen* 73(51): 4513-4514; 1976.

The direct relationship between number of cigarettes smoked and lung cancer risk, the nearly exclusive occurrence of lung cancer due to metaplasia of the columnar epithelium of the bronchial mucosa among smokers, and the nearly complete absence of this type of lung cancer among nonsmokers all attest to the etiological role of smoking in lung cancer and argue against the genetic hypothesis. The facts that lung cancer is practically unknown among nonsmoking Mormons and Seventh-Day Adventists and that lung cancer incidence has been increasing only during the last three decades or so refute the genetic theory. There is, however, one genetic factor predisposing for lung cancer. The activity of arylhydrocarbon hydroxylase (AHH), which converts benzo(a)pyrene into a highly carcinogenic metabolite, is determined genetically. Lung cancer incidence was found to be higher among smokers with high AHH activity than among smokers with low activity. (4 refs.)

77-4810 **Asbestos and Lung Cancer: An Analysis of the Epidemiological Evidence on the Asbestos-**

Smoking Interaction. (Eng) Saracci, R. (International Agency Res. Cancer, 150, cours Albert Thomas, 69008 Lyon, France). *Int J Cancer* 20(3): 323-331; 1977.

Three interaction mechanisms (models) between smoking and asbestos, both recognized as causes of lung cancer in man and animals, are proposed. According to the first model, the independent effects of asbestos and smoking added together are the same as those when both are present (additive model). The second model is a multiplicative (synergistic) model in which the addition of the second agent produces an effect that is proportional to the effect of the first. For example, if smoking alone increases the natural incidence of lung cancer 10 times and asbestos alone increases it 3 times, the incidence in those exposed to both will be 10 x 3, or 30 times the natural incidence. In the third model, asbestos can only increase lung cancer incidence in the presence of smoking. Detailed analysis of the five available epidemiological studies that provide information on occupational asbestos exposure, smoking habits, and lung cancer risk indicates that the multiplicative model is the most plausible and the additive model the least plausible. The mulitplicative model agrees with the mechanism of carcinogenesis that involves a multistage chain of discrete carcinogenic "hits" and with rat studies in which asbestos fibers were demonstrated to produce lung cancer. (32 refs.)

77-4811 **Biological Action of Asbestos.** (Rum.) Pilat, L. (Catedra de Medicina Muncii, I.M.F., Bucharest, Romania). *Rev Ig [Pneumoftiziol]* 26(1): 7-13; 1977.

Pneumoconiosis, lung cancer, pleural and peritoneal mesothelioma, pleural plaques, pleurisy, and, possibly, laryngeal and digestive tract cancers are induced by inhaled asbestos in occupationally exposed subjects. (25 refs.)

77-4812 **Cell Membranes in Cytotoxicity.** (Eng) Allison, A. C. (Clinical Res. Centre, Harrow, Middlesex England); Ferluga, J. *Adv Exp Med Biol* 84: 231-246; 1977.

The mechanisms of action of a variety of cytotoxic agents on cell membranes are discussed. Silica particles (silicon dioxide) are cytotoxic to macrophages because of their interaction with membranes surrounding secondary lysosomes. Silica also has a hemolytic effect via formation of hydrogen bonds with membrane phospholipid. Silicic acid (hydrated silica) contains hydroxyl groups that form hydrogen bonds with phosphate ester groups of phospholipids, thereby distorting membrane configuration and producing nonosmotic lysis. All types of asbestos are carcinogenic and fibrogenic. Chrysotile asbestos has magnesium hydroxide groups on its surface that may interact electrostatically with sialic acid groups of the membrane, increasing passive permeability to cations, which leads to osmotic lysis. The terminal components of complement (C5b to C9) insert into the membrane bilayer to increase the passive cation flux, producing osmotic lysis. Component C3a is highly toxic for many tumor cells. The mechanism by which T lymphocytes kill tumor cells is also discussed. Lymphocyte plasma membranes exhibit a cytotoxic potential that is dependent on a membrane-associated proteinase. (52 refs.)

77-4813 **Beryllium in the Environment.** (Eng) Reeves, A. L. (Sch. Medicine, Wayne State Univ. Detroit, MI 48202). *Clin Toxicol* 10(1): 37-48; 1977.

Industrial exposure to beryllium resulting in berylliosis is discussed. In toxicologic experiments in animals, beryllium produced pulmonary carcinomas in rats and monkeys after inhalation and bone sarcomas in rabbits after inhalation or iv injection, but guinea pigs showed no malignant changes after injection or inhalation. Evidence thus far implies that humans, like the guinea pig, are susceptible to berylliosis but resistant to beryllium induced cancer. (125 refs.)

77-4814 **Methyl Iodide.** (Eng) IARC Working Group *In: IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man: Some Fumigants, the Herbicides 2,4-D and 2,4,5-T, Chlorinated Dibenzodioxins and Miscellaneous Industrial Chemicals.* (Lyon: International Agency for Research on Cancer): Vol. 15, pp. 245-254; 1977.

Data on the carcinogenicity of methyl iodide are reviewed. Local sarcomas with pulmonary metastases were observed in BD rats who received single or multiple sc injections of the compound. In A/He mice, ip administration induced pulmonary lesions; but the small number of animals used prevented a thorough evaluation of carcinogenicity. No data on embryotoxicity or teratogenicity were available for study. The toxic effects of this compound in man are outlined; no case reports or epidemiological studies of human cancer were available. (36 refs.)

77-4815 **Hexamethylphosphoramide.** (Eng) IARC Working Group *In: IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man: Some Fumigants, the Herbicides 2,4-D and 2,4,5-T, Chlorinated Dibenzodioxins and Miscellaneous Industrial Chemicals.* (Lyon: International Agency for Research on Cancer): Vol. 15, pp. 211-222; 1977.

The experimental data on the carcinogenicity of hexamethylphosphoramide are reviewed. The compound induced squamous cell carcinomas of the nasal cavity in Charles River CD rats in inhalation experiments; tests with po administration in Sherman rats showed some tumor incidence, but these results were inconclusive. Other relevant data on hexamethylphosphoramide toxicity are presented. The compound did not produce chromosome aberrations in cultured human WBC; no epidemiological data on carcinogencity in humans were available. (46 refs.)

77-4816 **Acrylonitrile.** (Eng.) Finklea, J. F. (Natl. Inst. Occupational Safety and Health, 5600 Fishers Lane, Rockville, MD 20852). *Am Ind Hyg Assoc J* 38(9): 417, 419, 421-422; 1977.

The results of epidemiological studies linking occupational exposure to acrylonitrile with carcinoma of the colon and lung are reviewed, along with the results of feeding and inhalation studies in laboratory animals. Chemical companies should be alerted to the possible health hazards of acrylonitrile and proper protective measures should be instituted. (3 refs.)

77-4817 **Biochemistry of Occupational Cancer.** (Eng) Boyland, E. (TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, Keppel St., London WC1E 7HT, England). *J Soc Occup Med* 27(3): 97-101; 1977.

Environmental, particularly occupational, causes of cancer are reviewed briefly in terms of chemical reactions and intermediates. Chemical carcinogens can be divided into two groups on biochemical grounds. The first group, which includes alkylating agents such as mustard gas, nitrogen mustard, Myleran, and the ethyleneimines plus related compounds, acts directly without metabolic transformation. The second group, including aromatic amines, nitrosamines, polycyclic hydrocarbons, aflatoxin, safrole, and carbon tetrachloride, requires metabolic activation, usually through the formation of epoxides or arene oxides, to carcinogenic forms. Recent studies have indicated that vinyl chloride, chlorobutadiene, and trichloroethylene are carcinogenic and are metabolized through epoxide intermediates. Some ethylene derivatives or unsaturated compounds, therefore, can be carcinogenic because they are metabolized to epoxides. Saturated compounds such as trichloroethane and tetrachloroethane may be less hazardous than the unsaturated trichloroethylene and tetrachloroethylene as solvents. (no refs.)

77-4818 **Vinyl Chloride: Its Impact on Occupational Medicine Practice in Iran.** (Eng) Aryanpur, J. (Public Health & Occupational Medical Services, Natl. Iranian Oil Company, P. O. Box 1863, Tehran, Iran). *J Occup Med* 19(10): 689-692; 1977.

Measures taken to protect the workers at the Abadan Petrochemical Company in Iran from the carcinogenic effects of vinyl chloride monomer (VCM) and polyvinyl chloride (PVC) are outlined. Since 1971, all workers have been required to undergo periodic medical examinations with an emphasis on liver function. Factors related to liver disease, such as endemic viral hepatitis, low alcohol and cigarette consumption, and dietary habits, are considered. To date, among 43 workers in the VCM and PVC production units, none have evidence of liver dysfunction or angiosarcoma. The threshold limit value for VCM has been set at 25 ppm time weighted av for 8 hr with revisions expected in the future. No leakage to the community has been detected except for some chlorine release. (11 refs.)

77-4819 **Liver Endoplasmic Reticulum: Target Site of Halocarbon Metabolites.** (Eng) Reynolds, E. S. (Dept. Pathology, Peter Bent Brigham Hosp., Boston, MA 02115). *Adv Exp Med Biol* 84: 117-137; 1977.

The hepatotoxic effects of carbon tetrachloride, vinyl chloride, trichloroethylene, and halothane are reviewed. Initial injury produced by exposure to these chemicals involves the endoplasmic reticulum. There is dispersion of the ergastoplasm, then vacuolization and degranulation of the rough endoplasmic reticulum with concomitant retraction of the smooth endoplasmic reticulum into tightly clumped tubular aggregates. Membranes in these tubular aggregates seem to undergo supramolecular disassembly. This structural disorganization is accompanied by a diminished functional capacity in the organelle. Activation of these halocarbons to toxic species by the endoplasmic reticulum is indicated (1) by the enhancement of their toxicity upon pretreatment with chemicals, such as phenobarbital, or Aroclor 1254 that induce components of the mixed function oxidase system and (2) by the formation of certain metabolites and/or covalently bound products. It is not clear whether the halocarbons cause liver injury by the covalent binding of free-radical metabolites to tissue macromolecules or by initiating lipid peroxidation. (51 refs.)

77-4820 **The Induction of Liver Cell Cancer by Chemicals.** (Eng.) Wogan, G. N. (Dept. Toxicology, Massachusetts Inst. Technology, Cambridge, MA 02139). *In: Liver Cell Cancer.* Cameron, H. M.; Linsell, D. A.; Warwick, G. P., eds. (New York: Elsevier Scientific Publishing Co.): pp. 121-152; 1976.

Of the various known chemical hepatocarcinogens, the strongest evidence of involvement in human liver cancer exists for the aflatoxins. Others that may be involved include sterigmaticystin and, possibly, other mycotoxins; certain pyrolizidine alkaloids; cycasin and related glycosides; and ome nitrosamines and nitrosamides. (104 refs.)

7-4821 **Metabolic Activation of Mycotoxins by Animals and Humans: An Overview.** (Eng.) Shank, R. C. (Community Environmental Medicine, Medical Pharmacology and Therapeutics, Coll. Medicine, Univ. Caliornia, Irvine, CA 92717) *J Toxicol Environ Health* 2(6): 229-1244; 1977.

Comparative studies of the metabolism of aflatoxins in relaion to their carcinogenicity are reviewed. Early studies using ^{4}C-ring-labeled or methoxy-labeled aflatoxin B$_1$ (AFB$_1$), the most potent carcinogen of the group, suggested that the ring tructures of AFB$_1$ are stable but that the compound is rapidy O-demethylated in the rat. Five hydroxy derivatives or metabolites of AFB$_1$ (AFP$_1$, AFM$_1$, AFB$_2$a, AFQ$_1$, and AFR$_0$) appear to be involved in detoxification pathways. The comparative toxicity, carcinogenicity, and metabolism of AFB$_1$ for 12 species are summarized. Species highly sensitive to liver cancer are characterized by a slow rate of AFB$_1$ metabolism at high doses. Epoxidation of the 2,3-double bond in the terminal furan ring of AFB$_1$ apparently results in the active metabolite AFB$_1$ 2,3-epoxide. This epoxide decomposes to form a carbonium ion at C-2 that attacks neutrophilic sites n DNA, especially on the guanine moiety. Thus, AFB$_1$ appears to be activated to an alkylating agent in a manner similar to that of carcinogenic N-nitroso compounds and polycyclic hydrocarbons. (75 refs.)

77-4822 **Interrelationships of Mycotoxins with Nutrition.** (Eng.) Hamilton, P. B. (Dept. Poultry Science, North Carolina State Univ., Raleigh, NC 27607). *Fed Proc* 36(6): 1899-1902; 1977.

The interactions of mycotoxins with lipid, protein, carbohydrate, and vitamin nutrition are reviewed, with emphasis on aflatoxin and carcinogenicity. High-lipid diets have a mortality-sparing effect against aflatoxicosis; diets high in unsaturated fats have a growth-sparing effect. (40 refs.)

77-4823 **You Are What You Eat.** (Eng.) Nisbet, I. C. (Massachusetts Audubon Society, MA) *Technol Rev* 79(7): 5, 16-17; 1977.

The environmental, economic, and health effects of eating large amounts of meat are discussed. Several potentially carcinogenic chemicals are concentrated in animal fats, including residues of soil insecticides (dieldrin, heptachlor, chlordane); residues of synthetic hormones such as diethylstilbestrol, used to promote wt gain in cattle; and dioxins (toxic contaminants of range herbicides). Recent evidence suggests an association between current patterns of cancer incidence and meat consumption. The statistical association is becoming steadily clearer, but definite evidence for a cause-and-effect relationship is still weak. It is not clear whether the causative agents are animal fats, the meats themselves, diets low in fibers, preservatives, contaminants, or other factors associated with Western diets. (no refs.)

77-4824 **Diet and Cancer: Questions and Answers.** (Eng) Weisburger, J. (NCI Conference on Cancer Epidemiology and the Clinician, Boston, MA); Hill, P. *Cancer [Suppl]* 39(4): 1827-1828; 1977.

The association between diet and cancer is discussed. The various topics include the association between fat intake and colon and breast cancer, the difference between fat-induced and carbohydrate-induced obesity, exposure to nitrogen fertilizer and upper gastrointestinal cancer, and the protective effect of either Vitamin A or E in gastrointestinal cancer. (no refs.)

77-4825 **The Dietary Environment and Cancer.** (Eng) Wynder, E. L. (American Health Foundation, New York, NY). *J Am Diet Assoc* 71(4): 385-392; 1977.

The various associations between nutritional deficiencies and cancer are reviewed. The association between heavy alcohol intake and cancer of the upper alimentary tract is discussed, along with cancer of the larynx in smokers. Data suggest that alcohol acts as a tumor enhancer and not as a carcinogen; it is also suggested that nutritional deficiencies, such as a vitamin B deficiency, make the epithelial cells more susceptible to tobacco carcinogenesis. Foods high in dietary fat have been implicated in colon cancer, while high carbohydrate-low ascorbic acid diets have been implicated in gastric cancer. Consumption of lettuce and other green vegetables and fruits apparently lowers the risk of gastric cancer. It is suggested that ascorbate inhibits nitrosamine formation thereby reducing gastric cancer risk. Dietary fat has an effect on prolactin production and release and may thus be correlated with breast cancer. Furthermore, with dietary procarcinogens accumulated in the breast fluid, prolactin modification may act as a permissive agent in the transformation process. There is a positive association between dietary fat and colon cancer. Bowel transit times may have no influence in these cases; rather, various substances in the bile acids may act as promoters for unknown carcinogens. It is suggested that a diet similar to that recommended for the prevention of cardiovascular disease may help prevent certain cancers. (51 refs.)

77-4826 **Prenatal Oncogenesis and the Development of Malignant Tumors in the Infant and Adolescent Vagina--A Review and Hypothesis.** (Eng) Hilgers, R.D.(Div. Gynecologic Oncology, Univ. New Mexico Sch. Medicine, Albuquerque, NM 87131). *Gynecol Oncol* 5(3): 262-272; 1977.

Prenatal oncogenesis and, in particular, the association between clear-cell adenocarcinoma and maternal exposure to diethylstilbestrol (DES), with its implication of transplacental carcinogenesis, were reviewed. Epidemiologic observations of relationships among childhood neoplasms, genetic abnormalities, congenital tumors, and congenital malformations revealed that pathogenesis can occur during intrauterine development and that a temporal relationship may exist between teratogensis and oncogenesis. Intrauterine development is divided into an embryonic period and a fetal period. Nonspecific effects of transplancental chemical carcinogens are believed to be embryonic very early in development, teratogenic during organogenesis, but carcinogenic only during histogenesis and functional maturation of tissues during the fetal or neonatal periods. Thus, teratogenesis precedes carcinogenesis, and when organogenesis is completed, carcinogenesis predominates. Oncoteratogenesis may explain the effect of DES; teratogenic changes resulting from prenatal exposure to DES may require a later postnatal mutagenic event to occur before oncogensis occurs. DES appears to act primarily as a teratogen and not as an oncogen. Also discussed are the malignant neoplasms that develop in the subepithelial connective tissue layer of the human vagina during the first two decades of life. These include embryonal rhabdomyosarcomas, endodermal sinus tumors, and clear-cell adenocarcinomas. (49 refs.)

77-4827 **Cancer Induction by Exogenous Hormones: Questions and Answers.** (Eng) Pike, M.(NCI Conference on Cancer Epidemiology and the Clinician, Boston, MA); Segaloff, A.; Greenwald, P. *Cancer [Suppl]* 39(4): 1899-1900; 1977.

The role of exogenous hormones in the induction of human cancer is discussed. Particular attention is paid to oral contraceptives, especially mestranol, implicated in the development of hepatic adenomas and hepatic focal nodular hyperplasia. The continued use of diethylstilbestrol during pregnancy is considered. (no refs.)

77-4828 **Cancer Risks from Estrogen Intake.** (Eng) Greenwald, P. (New York State Dept. Health, Cancer Control Bureau, Tower Building, Empire State Plaza, Albany, NY 12237); Nasca, P. C.; Caputo, T. A.; Janerich, D. T. *NY State J Med* 77(7): 1069-1074; 1977.

Evidence on the possible cause-and-effect relationship of estrogens to cancer is reviewed, and measures that can be taken to insure the early recognition of estrogen-associated tumors are recommended. Previously published data are related to cancer trends in New York State, where 22 teenage or young adult women with adenocarcinoma of the vagina have been reported. Eighteen of these women have documented in utero exposure to diethylstilbestrol or another synthetic estrogen. Ten of the patients have died of advanced disease. More than 250 such patients have been reported for the entire country, and new cases will probably continue to be found, perhaps with increasing frequency before leveling off. Oral contraceptives have not been shown to increase cancer risk, but insufficient time has passed since they came into common use in the mid-1960's to make a conclusive judgment about their safety. In New York State there has been a rapid rise in endometrial cancer since 1970, which follows a major increase in the frequency of menopausal estrogen use at least 10 yr earlier. Epidemiological studies show a strong positive association between estrogen use and endometrial cancer. One study has also found increased breast cancer risk following menopausal estrogen use. Women taking estrogens should have frequent pelvic cancer-screening examinations. Patients at high risk or with a suspicious history should also have an evaluation of the endometrial cavity. (30 refs.)

77-4829 **Saccharin and Chemical Carcinogenesis.** (Eng.) Anonymous (No affiliation given). *Med Lett Drugs Ther* 19(18): 75-76; 1977.

Although saccharin has been shown to be carcinogenic in rats and mutagenic in bacteria, there is no conclusive evidence on its carcinogenicity in man. The belief that the risk of carcinogenesis is small should not be encouraged until the degree of risk is determined. Perhaps in humans cancer risk to sites other than the bladder may be increased by saccharin. (8 refs.)

77-4830 **Malignant Melanoma in a Thermal Burn Scar (Letter to Editor).** (Eng.) Gellin, G. A. (San Francisco, CA); Epstein, W. L. *Arch Dermatol* 113(9): 1295; 1977.

Malignant melanoma has been reported in a 47-yr-old fireman who was burned on duty. A search of the literature revealed two other cases of malignant melanomas arising in burn scars, but whether these burns were thermal or chemical could not be ascertained from existing records. (3 refs.)

77-4831 **The Role of Inert Foreign Bodies in the Pathogenesis of Cancer (Letter to Editor).** (Eng.) Ecanow, B. (Univ. Illinois at the Medical Center, Chicago, IL 60612); Gold, B. H.; Sadove, M. *Br J Cancer* 36(3): 397; 1977.

"Inert" particles within the body do "act" by adsorbing films of surface-active molecules on normal cell surfaces. Adjacent films adhere to each other, forming a matrix between the inert body and the cells. As the matrix becomes more immobilized, its physicochemical properties are altered; and eventually the metabolism of the cells is altered. It is this change that can result in cancer. (5 refs.)

77-4832 **Ionizing Radiation Causing a Risk of Cancer in Man. A Short Review and a Discussion.** (Eng) Fichardt, T. (Dept. Radiotherapy, H. F. Verwoerd Hosp., Pretoria, S. Africa); Sandison, A.G.; Savage, D. J. *S Afr Med J* 52(8): 321-327; 1977.

A review is presented of some of the most important etiologic agents implicated in the development of human cancer at various organ sites; these include alcohol, tobacco smoke, sunlight, hormones, bacteria, viruses, and various industrial chemicals. Epidemiological studies of radiation-associated cancers, resulting from occupational, therapeutic or atomic bomb exposure, are discussed. Although ionizing radiation may be carcinogenic to certain sites, such as the lymphatic and hematopoietic tissues, its intelligent use in diagnosis and therapy poses a minimal risk. There are no substantiated reports in the literature to prove that ionizing radiation is involved in the etiology of the eight major primary cancers that affect man today (cancer of the esophagus, stomach, colon, liver, lung, breast, uterus, and prostate). (56 refs.)

77-4833 **X-ray Therapy and Cancer of Other Sites.** (Eng.) Katz, J. H. (Dept. Dermatology, Cornell Univ. Medical Coll., New York, NY). *CA* 27(2): 117-118; 1977.

Although basal cell carcinoma of the head and face may be caused by therapeutic superficial X-irradiation to these sites, there is no evidence that the radiation increases the cancer risk to any other organ system. Exposure to sunlight may also be involved in skin cancers in irradiated patients. (2 refs.)

77-4834 **Genetic Damage from Diagnostic Radiation (4 Letters to Editor).** (Eng.) Gould, L. V. (Upstate Medical Center, Syracuse, NY); Bledsoe, T. R.; Land, C. E.; Oppenheim, B. E. *JAMA* 238(10): 1023-1025; 1977.

Radiologists are aware of the risk associated with low level radiation as well as the benefits of diagnostic x-ray procedures. A model for interpreting epidemiological data has shown a 50-fold increased risk of pediatric leukemia in children genetically damaged by exposure to radiation in utero; however, the fit of the model to the data and the calculations thus obtained are criticized on several accounts. (5 refs.)

77-4835 **Selected Safety-related Occurrences Reported in March and April 1977.** (Eng.) Castro, W. R. (No affiliation given). *Nucl Saf* 18(4): 548-552; 1977.

Several incidents involving occupational exposure to radioactivity are reported. (6 refs.)

77-4836 **Occupational Radiation Exposures at Licensed Facilities, 1975.** (Eng) Brooks, B. G. (Operating Data Branch, U.S. Nuclear Regulatory Commission). *Nucl Saf* 18(4): 523-527; 1977.

Personnel occupational radiation exposures for 1975 were obtained from reports submitted by 387 Nuclear Regulatory Commission licensees, including nuclear power reactors; industrial radiographers; and fuel and byproduct processors, fabricators, and reprocessors. In this summary report, only exposure distribution information, man-rems for the reporting categories, and a summary of exposures at licensed power-reactor facilities are included. A total of 78,713 individuals, who incurred an av exposure of 0.36 rem, were monitored during 1975. From 1968 to 1975, > 95% of the exposures were < 2 rems and few exposures exceeded 12 rems (allowable annual limit). The distribution of the cumulative doses among the major work functions of workers at power-reactor facilities showed that in 1975, routine maintenance continues to be the major contributor, with 52.6% of the cumulative dose, followed by special maintenance with 19.0%. (10 refs.)

77-4837 **Protective Ozone Layer (Letter to Editor).** (Eng.) Maclay, W. N. (Monroeville, PA). *Chem Eng News* 55(30): 2; 1977.

The ozone layer limits penetration by carcinogenic UV radiation through a self-regulatory mechanism: increased radiation produces additional ozone. Thus, chlorofluorocarbons from aerosol cans do not threaten to destroy the ozone layer; however, their vapors are harmful to inhale. (no refs.)

77-4838 **The Relation Between Induced Mutation Frequency and Cell Survival-- A Theoretical Approach and an Examination of Experimental Data for Eukaryotes.** (Eng.) Munson, R. J. (M. R. C. Radiobiology Unit., Harwell, Didcot, Oxon OX11 ORD, England) Goodhead, D. T. *Mutat Res* 42(2): 145-160; 1977.

Many mutagens (eg, x-rays, UV rays, chemicals) are known to induce a variety of lesions in DNA. Cellular repair systems may eliminate some of these, but some unrepaired lesions may lead to loss of reproductive capacity and others to viable mutations. Simple considerations of these three alternative fates of an exposed cell show that there should be a linear relation between the logarithm of the surviving fraction (log S/S_0) and log(1 - M), where M is the mutant frequency. For low frequencies the relation assumes the simpler form $M = -m \log S/S_0$. The published literature on experimental mutagenesis in eukaryotes confirms these expectations. Observed differences in the slope *m* when different mutagens induce the same mutation in a given kind of cell (or a given mutagen induces the same mutation in different kinds of cells) imply that mutation and cellular inactivation do not arise from one type of DNA lesion only. (30 refs.)

77-4839 **DNA Repair and Tumours of the Skin: Xeroderma Pigmentosum as a Model.** (Eng.) Giannelli, F. (Guy's Hosp. Medical Sch., London SE1 9RT, England). *Proc R Soc Med* 70(6): 388-395; 1977.

Defects in DNA repair mechanisms in xeroderma pigmentosum (XP) are discussed. The absorption of photons by the DNA leads to a variety of chemical changes, the most frequent one being the formation of pyrimidine dimers that produce large distortions in the DNA molecule. Human cells rely essentially on excision repair for the removal of pyrimidine dimers. Approximately 80%-90% of all XP patients are defective in excision repair and most probably in its first step, the recognition of lesions and the incision of DNA. There is a high degree of genetic heterogeneity in XP patients, which emphasizes the fact that many genes are involved in the maintenance of DNA. A group comprising 10%-20% of XP patients shows normal excision but defective postreplication repair. This group (XP variant) is clinically indistinguishable from the rest. The phenotype of XP and XP variants permits the conclusion that distinct metabolic defects impairing either the removal of pyrimidine dimers or the bypass of these lesions during RNA replication result in susceptibility to actinic cancer. There are three hypotheses on how DNA damage leads to malignant transformation: (1) DNA damage acts by causing mutations; (2) DNA damage favors virus-induced cell transformation; and (3) cellular sensitivity to UV light, caused by defects of DNA repair, may favor tumor growth in several indirect ways. Most studies have provided evidence for the influence of mutations on the origin of XP-related cancer, but experimentation to test the other hypotheses is still needed. (50 refs.)

77-4840 **The Effects of Radiation on the Immune Response: A Review.** (Eng) Markoe, A. M. (Dept. Radiation Therapy and Nuclear Medicine, Hahnemann Medical Coll. and Hosp., Philadelphia, PA); Saluk, P. H. *Appl Radiol* 6(5): 63, 66-72, 122; 1977.

A review of the effects of radiation on the immune system is presented, with emphasis on clinical experience and additional reference to animal studies where necessary. The immunocompromised cancer patient and the immunosuppressive effects of radiation therapy for malignant disease are discussed. The differential susceptibility of various cellular components to radiation is considered and related to cellular response. (43 refs.)

77-4841 **Transfer RNA in RNA Tumor Viruses.** (Eng) Waters, L. C. (Carcinogenesis Program, Biology Div., Oak Ridge National Lab., Oak Ridge, TN); Mullin, B. C. *Prog Nucleic Acid Res Mol Biol* 20: 131-160; 1977.

The presence of transfer RNA (tRNA) in RNA tumor viruses and the content, composition, and possible and probable functional roles of this viral tRNA are discussed and reviewed. The 4S tRNA molecules have been found to be associated with the 70S and 35S RNA of these viruses, as well as to exist in a "free" form. The free tRNA content of various viruses differs significantly from that of their lost cells and from each other, with the predominance (approx 10%-30%) of one or a few types. Specific viral tRNA's appear to serve as primers, or initiators of viral DNA synthesis. Homologies between tRNA and 35S RNA are known; therefore, tRNA may serve as a link between 35S RNA's as well as a primer for reverse transcriptase. Additional possible functions of the viral tRNA's are as part of a viral translational apparatus and as modulators of cellular protein synthesis. (169 refs.)

77-4842 **RNA Viruses and Cancer. Lucy Wortham James Lecture (Basic Science).** (Eng.) Temin, H. M. (McArdle Lab. Univ. Wisconsin, Madison, WI 53706). *Cancer* 39(2): 422-428; 1977.

A review is presented of the relationship of some RNA viruses to cancer, how some of these viruses cause cancer in chickens, and how understanding more about replication and evolution of these viruses may provide an analogy for the action of non-viral carcinogens. It is proposed that non-viral carcinogens act to mutate a cellular gene(s) that is involved in a process of information transfer and genetic variation similar to that of viral components; this process results in the formation of cancer genes. (25 refs.)

77-4843 **Tumor Induction by Viruses.** (Ger) Fleckenstein, B. (Harvard Medical Sch., New England Regional Primate Res. Center, One Pine Hill Drive, Southborough, MA 01772). *Fortschr Med* 95(5): 275-277; 1977.

In this review of the literature on tumor virology, it was found that only 0.2% of the middle European tumor cases are virus-associated. Epidemiological studies have shown that 90% of the adult population in middle Europe have antibodies against Epstein-Barr virus (EBV), and they remain mostly asymptomatic, but it does cause infectious mononucleosis. In the past 20 yr, oncornaviruses have been isolated from human leukemias, lymphomas, and sarcomas. Others have reported oncornavirus-specific nucleic acids, structural proteins, and enzymes. Adenoviruses have caused nondifferentiated sarcomas in rodents, but no direct evidence of oncogenicity has been shown in humans. Infectious agents are presumed to be responsible for causing Burkitt's lymphoma. Burkitt's lymphoma only occurs in children who had an early primary EBV infection. Nasopharyngeal carcinoma has also been associated with EBV, whereas no correlation was found between diseases such as Hodgkin's disease. In vitro, EBV has induced lymphoproliferative neoplasias in some monkey lymphocytes. An elevated antibody titer against herpes simplex virus type 2 has been detected in patients with cervical cancer, and in vitro tests have demonstrated the oncogenicity of this virus. Other viruses that have been implicated include cytomegalovirus and papovavirus. (9 refs.)

77-4844 **The Inhibition of Cell Functions after Viral Infection. A Proposed General Mechanism.** (Eng.) Carrasco, L. (Dept. Molecular Virology, Imperial Cancer Res. Fund, London WC2A 3PX, England). *FEBS Lett* 76(1): 11-15; 1977.

Several observations and explanations of the shut-off phenomenon (inhibition of host-cell protein synthesis) which follows viral infection are presented. In addition, a membrane-leakage model is proposed, which not only explains this shut-off phenomenon, but may also explain the spectrum of different effects observed after viral infection. (36 refs.)

77-4845 **Oncogenic Virus Host Cell Relationships.** (Ger.) Munk, K. (Institut fur Virusforschung, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, D-6900 Heidelberg, W. Germany). *Munch Med Wochenschr* 119(10): 323-324; 1977.

The virus-host cell relationship is reviewed. DNA-containing oncogenic viruses, such as simian virus 40, can enter into the virus-host cell relationship without proliferating. The viral DNA incorporated into the cell controls cell function, giving it the characteristic of a malignantly transformed cell. Thus, a tumor is formed. Herpes simplex virus functions in this manner and can remain latent for a long time. (19 refs.)

77-4846 **Viral Attributes and Host Factors in Carcinogenesis: Herpesviruses.** (Eng) Joncas, J. H. (Institut Armand-Frappier 531, Blvd. des Praries, C. P. 100, Laval-des-Rapides, Quebec, Canada H7N 4Z3). *Rev Can Biol* 36(1): 17-25; 1977.

Two different phenomena are considered: (1) congenital cytomegalovirus (CMV) infection and the properties of lymphoblastoid cell lines derived from the peripheral blood of an infant with congenital CMV infection; and (2) the occurrence of multiple cases of Burkitt's lymphoma and nasopharyngeal carcinoma (NPC) in one family. Serological evidence of congenital Epstein-Barr virus (EBV) was also obtained from the infant with CMV infection, but the possibility of double congenital infection could not be established conclusively. One of the lymphoblastoid cell lines derived from this infant contained an unexpressed CMV genome in addition to the EBV. EBV antigens, but not CMV antigens, could be detected in the lymphoblastoid cell lines. Two lymphoblastoid cell lines positive for CMV by molecular hybridization synthesized large amounts of intracytoplasmic IgM. This IgM production may be under the control of the virus genome. In the family situation, all members were EBV viral capsid antigen (VCA)- and nuclear antigen (EBNA)-antibody positive. The two members with NPC had high titers of EBV-VCA, early antigen (EA), and EBNA antibodies. The only other member of this family that had EBV-EA antibodies was the mother. Borderline IgA deficiency was seen in three members. It is speculated that the host intracellular resistance mechanisms and the immunological surveillance mechanisms are much more decisive than the viral attributes in the outcome of the host-virus challenge, whether cancer or infectious disease is the result. (24 refs.)

77-4847 **The Pathogenesis and Therapy of Tumors.** (Ita.) Guarino, A. (No affiliation given). *Bull Scie Med (Bologna)* 149(1): 36-39; 1977.

The viral induction of cancer is discussed in light of the immunological defenses of the body. (1 ref.)

77-4848 **Recent Progress in Epstein-Barr Virus Research.** (Eng) Epstein, M. A. (Dept. Pathology, Univ. Bristol, Medical Sch., University Walk, Briston B58 BS8 1TD, England); Achong, B. G. *Annu Rev Microbiol* 31: 421-445; 1977.

A review is presented of recent research findings with Epstein-Barr virus (EBV) suspected as a causative agent in African Burkitt's lymphoma and nasopharyngeal carcinoma. The following topics are included: the virus-determined antigens (lymphocyte-defined membrane antigen, EB nuclear antigen, membrane antigen, early antigens, virus capsid antigens), variations in host antibody responses, types of infections and antigen expression in human B cells in vivo, EBV DNA and its relation to host cell DNA, origin of various EBV-containing human lymphoblastoid lines, antigens in EBV containing human lymphoblastoid lines, EBV-negative human lymphoblastoid lines, infectible cells and virus receptors, human lymphoid cells and tumor induction in rodents, different strains of EBV, chromosome studies, EBV and neoplasia, EBV and tumor-free individuals, and the significance of oncornaviruses in EBV-transformed cells. Studies with Burkitt's lymphoma indicate that the EBV has more than a passenger role in the genome; studies with nasopharyngeal carcinoma suggest that EBV reacts with an unknown environmental and/or genetic cofactor. It is postulated that target cells with specific responses, perhaps genetically determined, undergo malignant change induced by EBV. The nature of this transformation process in vivo is likely to parallel the mechanisms observed in vitro. (247 refs.)

77-4849 **Viruses and Cancer Clusters: Questions and Answers.** (Eng) Grufferman, S. (NCI Conference on Cancer Epidemiology and the Clinician, Boston, MA); Hardy, W.; Pike, M. *Cancer [Suppl]* 39(4): 1856-1860; 1977.

The role of viruses in human cancers is discussed. The associations between herpes virus and cervical cancer, feline leukemia virus and lymphosarcoma in cats exposed to the leukemia virus, the Gallo agent and acute myelogenous leukemia, and Burkitt's lymphoma and Epstein-Barr virus are considered, along with the possible infectious etiology of Hodgkin's disease. (no refs.)

77-4850 **The Mouse Myeloma System. A Model for Studying the Effect of Malignant Transformation of Immunoglobulin Production.** (Eng.) Baumal, R. (Dept. Immunology, Res. Inst., Hosp. for Sick Children, Toronto, Ontario, Canada); Percy, M. *Isr J Med Sci* 13(8): 777-796; 1977.

The use of mouse myeloma cells, which continue to produce immunoglobulin (Ig) despite extreme cellular atypia, to study the structure and production of Ig is discussed. In biosynthesis studies, myeloma cells were incubated in vitro with radioactive amino acids or sugars for variable periods of time. Following a series of preparative steps, the intracellular and secreted Ig molecules and intermediates were separated and identified by electrophoresis on sodium dodecyl sulfate polyacrylamide gels or on alkaline urea-polyacrylamide gels. These techniques in conjunction with subcellular fractionation showed that there are two different size classes of polyribosomes within Ig-forming myeloma cells. Heavy (H) chains are associated with the larger (270S) and light (L) chains with the smaller (190S) class. A large number of IgG-producing mouse myeloma tumors were studied in detailed pulse-chase experiments, which showed that most of the interchain disulfide bonds of Ig were formed after the ribosome stage, within 10-30 min following the pulse and chase. Pulse-chase studies with IgA- and IgM-producing mouse myeloma cells failed to show appreciable amounts of covalently bonded intracellular polymer. Other studies have indicated that noncovalent and covalent assembly occur in rapid succession. In some cells, probably as a result of malignant transformation, spontaneous production of defective H and/or L chains occurs, which may lead to aberrant Ig biosynthesis and secretion. Study of variant Ig production by these myeloma cells has led to a fuller understanding of Ig biosynthesis and secretion. (46 refs.)

77-4851 **The Problem of Immunity to Breast Cancers.** (Eng) Zimmermann, A. (Inst. Pathology, Univ. Bern, Bern, Switzerland); Ruchti, C.; Roos, B.; Cottier, H. *Prog Clin Biol Res* 12: 75-89; 1977.

Our current understanding of the problem of specific immunity toward human mammary carcinoma is reviewed. The roles of tumor-associated antigens, antigen recognition, and cell mediated and humoral-specific immune responses are discussed. Immunosurveillance appears to play a significant antitumor role, but the possibility of immunostimulation by, for example, a blocking antibody is considered. Developmental stages, characteristics (type, histological differentiation, antigenicity or immunogenicity, growth rate, glycolytic capacity, invasiveness, angiogenic capacity, degree of autonomy toward regulatory mechanisms) and progression of the neoplasms with alteration of the immune status of the host determine prognosis. Immunomorphological observations of primary breast cancer and regional lymph nodes correlated with other clinical observations. (44 refs.)

77-4852 **Derangements of Humoral Immunity in Malignancy (Meeting Abstract).** (Eng) Lewis, M. G. (McGill Univ., Cancer Res. Unit., McIntyre Medical Sciences Building, 3655 Drumond St., Montreal, Quebec H3G 1Y6, Canada); Phillips, T. M.; Hartmann, D.; Jerry, L. M. *Eur Surg Res* 9(4): 288-289; 1977. (9 refs.)

7-4853 **Experimental Models with Possible Implications for the Role of HLA in Malignancy.** (Eng) Villiams, R. M. (Div. Tumor Immunology, Dept. Medicine, Iarvard Medical Sch., Boston, MA 02115). *Prog Clin Biol Res* 16: 21-28; 1977.

The role of the major histocompatibility complex (MHC) in umor resistance and autoimmunity was investigated using wo laboratory systems. The rat disease experimental allergic ncephalomyelites (EAE) was used to study genetic control of autoimmunity, and the hybrid effect, or allogeneic inhibiion, in mice was used to study genetic control of resistance to histocompatible tumors. In the mouse studies, definite H-2 (MHC) effects were seen along with rather dramatic non-H-2 effects. After injection of the DBA/2 mastocytoma P815 into two H-2-identical strains that had different non-H-2 backgrounds, it was found that the C57BL/10 background offered significant advantage to the host with respect to duration of survival. An apparent H-2 effect was still noted when H-2d and H-2k, defined as nonresponder haplotypes, are compared with H-2a, a k/d recombinant, which is a responder. Study of genetic control of EAE by the rat MHC (H-l) showed the requirement of the MHC-linked Ir-EAE gene for EAE. Lewis rats (H-11) are uniformly susceptible to EAE, but Brown Norway (BN, H-1n) rats are resistant. Hybrids between these strains ($LBNF1_1$, H-12/H-1n) are uniformly susceptible, but they have less-severe lesions. One possible explanation for this is a gene dose effect for severity. But non-H-1-linked genes or an H-1-linked immune suppression gene, Is-EAE, may also be involved. There are numerous mechanisms by which the MHC may influence malignancy, and it is probable that combinations of more than one may be responsible for MHC regulation of autoimmunity and tumor growth. (13 refs.)

77-4854 **Alpha-chain Disease and Related Small-intestinal Lymphoma: A Memorandum.** (Eng) Immunology Working Group (World Health Organization, Ave. Appia, 1211 Geneva 27, Switzerland). *Bull WHO* 54(6): 615-624; 1977.

A review of immunoproliferative small intestinal disease (IPSID) is presented. The disease affects primarily young adults in the 20 to 40 yr age bracket; both sexes are affected equally. IPSID is most prevalent among residents of the Mediterranean region, South Africa, India, South and Central America. There appears to be no clustering of IPSID in families, and no potential etiological factors have been identified. Attempts to establish cell lines from patients with the disease have not been successful, and virological studies have not yielded any significant findings. Bacteriological and parasitological studies for peculiar organisms have not produced any significant result. The major presenting symptoms include chronic diarrhea, abdominal pain and distension, nausea, vomiting and wt loss. Histologically, diffuse plasma-cell infiltration occuring throughout the small intestine is usually confined to the mucosal lamina propria and may lack conclusive cytological features. The characteristic immunoglobulin abnormality found in IPSID patients is the defective alpha-heavy chain disease (αHCD) protein, consisting of incomplete heavy α-chains, devoid of light chains, with a mol wt between 29,000 and 34,000 daltons. The primary defect is attributed to a deletion affecting the variable and first constant regions of the heavy chains which are under independent control. Problems involved in identifying the αHCD protein in IPSID patients are discussed. (41 refs.)

77-4855 **Possible Effects of Growth Hormone on Development of Acute Lymphoblastic Leukaemia.** (Eng) Rogers, P. C. (Dept. Pediatrics, Health Center for Children, 715 W. 12th Ave., Vancouver, British Columbia, Canada); Komp, D.; Rogol, A.; Sabio, H. *Lancet* 2(8035): 434-435; 1977.

The possible role of growth hormone (GH) or a GH-dependent somatomedin in the process of acute lymphoblastic leukemia (ALL) is considered. GH has a trophic effect on lymphoid tissue and also specific receptors on lymphocytes, probably T cells. Hypophysectomy in rats with induced T-cell leukemia can suppress the leukemic process. Incubation of cultured lymphocytes with human GH increased the percentage of cells undergoing blastogenic transformation. Morphologically, the stimulated blast forms were typical lymphoblasts and not immunoblasts, suggesting increased stimulation of T rather than B cells. GH concentrations in some children with ALL were raised at initial diagnosis and at relapse, but they fell after remission. There was a significant decrease in somatomedin concentrations after vincristine and prednisone therapy during remission induction. It is suggested that control of GH and/or somatomedin concentrations may be necessary for adequate treatment of some cases of ALL in children. (10 refs.)

77-4856 **Steroid Hormone Receptors in the Regulation of Differentiation. A Review.** (Eng.) McCarty, Jr., K. S. (Dept. Pathology, Duke Univ. Medical Center, Durham, NC 27710); McCarty, K. S. *Am J Pathol* 86(3): 703-744; 1977.

Transport and availability of steroids for interaction with target cells are surveyed, evidence of steroid receptor activity is cited, and the clinical application of the steroid receptor theory to mammary, prostatic endometrial, and renal cell carcinomas and to lymphomas and lymphoblastic leukemia is discussed. (184 refs.)

77-4857 **Glucose-6-phosphate Dehydrogenase (G-6-PD) Markers in Burkitt Lymphoma and Other**

Malignancies. (Eng) Fialkow, P. J. (Medical Genetics, Medical Service, VA Hosp., Seattle, WA). *Haematol Blood Transfus* 20: 297-305; 1977.

Tumors in patients with genetic mosaicism were studied to gain information about their mode of origin and development. The x-linked glucose-6-phosphate dehydrogenase (G-6-PD) locus was used as a marker in women heterozygous for the usual B gene (*Gd*B) and a variant allele such as *Gd* A, with random inactivation of one x-chromosome in each somatic cell. Evidence was found that indicates a stem cell origin of several myeloproliferative disorders, including chronic myelocytic leukemia, polycythemia vera, and idiopathic myelofibrosis with myeloid metaplasia. These studies strongly suggest that these diseases have a single cell origin, ruling out several alternative etiolgies. Similar studies indicated that at least some benign hereditary and viral growths have a multicellular origin, but Burkitt's lymphoma, for which the putative causative agent is Epstein-Barr virus, has a clonal origin. Chromosome markers have demonstrated that some recurrences of acute lymphoblastic leukemia may be new occurrences of disease and have a multiple cell origin, suggestive of transfer or activation of an oncogenic virus. (47 refs.)

77-4858 **The Lympo-dependent Neoplasm (Meeting Abstract).** (Eng) Prehn, R. T. (Jacskon Lab., Bar Harbor, ME). *J Reticuloendothel Soc* 22(2): 97; 1977. (no refs.)

77-4859 **The Spread of Cancer in the Organism. Facts and Problems.** (Eng) Strauli, P. (Div. Cancer Res., Inst. Pathology, Univ. Zurich, CH-8050 Zurich, Switzerland). *Naturwissenschaften* 64(8): 403-409; 1977.

In a review of cancer spread and penetration, cancer is considered as a membrane disease which alters cell surface properties. With an impaired tissue affiliation in cancer cells, there is a reduction in cell adhesion. This loss can be incomplete, with spread as a consequence. With partial loss, the cancer penetrates adjacent tissue and proliferates. The tumor-host interface is the region of host response to the tumor. Tumor cells that have lost contact inhibition penetrate the lymph system and frequently become entrapped in the lymph nodes; these are regions of metastatic colonization. Blood-borne cancer elements entrapped in the capillaries may then proliferate or may become attached by other mechanisms. The organ selectivity of metastatic colonization coincides for the most part with a soil and seed model, or it may represent a nontoxicity of certain types of cancer cells to certain organs. (66 refs.)

77-4860 **Cellular Interaction as a Limiting Factor in the Expression of Oncogenic Mutations: A Hypothesis.** (Eng.) Riccardi, V. M. (Genetics Unit, Milwaukee Children's Hosp. Dept. Pediatrics, Medical Coll. Wisconsin, Milwaukee, WI 53233). *In: Genetics of Human Cancer.* Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F., eds. (New York: Raven Press): Progress in Cancer Research and Therapy Vol. 3, pp. 383-385; 1977.

Based on clinical observations of von Recklinghausen's neurofibromatosis, a hypothesis is presented that nonmutant cells have the ability to nullify the expression of an oncogenic mutation. A nongenetic determinant in the expression of certain somatic or germinal mutations is suggested. (6 refs.)

77-4861 **Ultrastructure of the Nuclear Membrane and Its Mitotic Lysis as a Hypothetical Factor of Precancerous Tumor Development.** (Ita.) Montaldo, G. (Centro di Microscopia Elettronica, Universita di Cagliari, Cagliari, Italy). *Pathologica* 69(987/988): 1-6; 1977.

The mitotic lysis and ultrastructure of the nuclear membrane are discussed as hypothetical factors of precancerous tumor growth. A large number of mitoses may render the nuclear DNA more susceptible to carcinogenic stimuli. (7 refs.)

77-4862 **'Foetalism' in Cancer: Towards the Evolution of a Unified Theory of the Initiation and Maintenance of the Cancerous State.** (Eng.) Longenecker, J. P. (Dept. Biochemistry, Sch. General Studies, Australian Natl. Univ., PO Box 4, Canberra, ACT, Australia 2600); Williams, J. F. *Cancer Forum* (11): 381-387; 1977.

The 'embryonic rest' hypothesis of tumorigenesis, which states that tumors are the result of embryonic cells that persist into adulthood and begin to proliferate, is reviewed. The evidence suggests that the trophoblast-like characteristics of malignant cells are the result of reactivation of developmental genomes. (56 refs.)

77-4863 **Retinoblastoma and Osteogenic Sarcoma.** (Eng) Francois, J. (Clinic Ophtalmologique, Academisch Ziekenhuis, De Pintelaan 135, B-9000 Ghent, Belgium). *Ophthalmologica* 175(4): 185-191; 1977.

A review of the literature showed that osteosarcomas accounted for 80% of the 85 reported radiogenic tumors in retinoblastoma patients and for 48% of the 23 nonradiogenic second neoplasms in these patients. There are also retinoblastoma families in which some members develop an osteosarcoma without retinoblastoma. The possible genetic significance of the association between the two tumors is discussed. (48 refs.)

77-4864 **Histogenesis of Fibroepithelial Tumors of the Mammary Gland with Special Regard to Cystosarcoma Phyllodes.** (Bul) Popov, E. (Medical Acad., Inst. Medical Biology, Bulgaria). *Onkologiia* 14(1): 35-42; 1977.

Literature on the histogenesis and etiology of fibroepithelial tumors of the mammary gland is summarized. Four stages can be recognized in the histogenesis of these tumors: disseminated plus globular, connective, and epithelial tissue hyperplasia; further globular hyperplasia; formation of the fibroadenomatous node; final formation of the nodes, with connective tissue involvement. The malignant variant of cystosarcoma phyllodes is histogenetically interrelated with sarcoma, the benign variant with fibroadenoma. (99 refs.)

77-4865 **Animal Model: Carcinogenesis in the Uterine Cervix in Mice.** (Eng) Rubio, C. A. (Inst. Pathology, Karolinska Sjukhuset, S-104 01 Stockholm, Sweden). *Am J Pathol* 88(3): 799-802; 1977.

Carcinogenesis in the uterine cervix in mice is an animal model of the human disease, and work in this area is reviewed. Preinvasive lesions in the cervix of C57BL mice were evoked by local application of 3,4-benzpyrene in 1% acetone twice a week for 5 mo. The graded series of cervical atypias that developed progressed with time, resulting in questionable or unquestionable carcinoma in 22% of the mice. Murine atypia Grade III (severe), believed to be the lesion from which invasive carcinoma of the cervix originates, showed a histologic pattern and biological attributes similar to those of human carcinoma in situ, a lesion found in > 90% of human patients with invasive cervical carcinoma. The remarkable similarity between carcinogenesis of the uterine cervix in mice and in humans strongly recommends the mouse as a model for the development of squamous carcinoma in that organ. (14 refs.)

77-4866 **The Pathology of Experimental Liver Cell Cancer.** (Eng.) Farber, E. (Dept. Pathology, Univ. Toronto, Faculty Medicine, Toronto, Ontario M5G 1L5, Canada). *In: Liver Cell Cancer.* Cameron, H. M.; Linsell, D. A.; Warwick, G. P., eds. (New York: Elsevier Scientific Publishing Co.): pp. 243-277; 1976.

Physiologic and pathologic changes in the liver that accompany chemical carcinogenesis are discussed. A major problem in carcinogenesis is the growth of hepatocytes in a carcinogen-induced environment in which normal cell proliferation is inhibited. The altered new cell populations that result have acquired a resistance to the cytotoxicity of carcinogens that may be a key factor in the selection of putative preneoplastic or premalignant hepatocytes. (227 refs.)

77-4867 **The Pathology of Liver Cell Cancer.** (Eng.) Cameron, H. M. (Dept. Pathology, Univ. Edinburgh, Teviot Place, Edinburgh EH8 9AG, Scotland). *In: Liver Cell Cancer.* Cameron, H. M.; Linsell, D. A.; Warwick, G. P., eds. (New York: Elsevier Scientific Publishing Co.) pp. 17-43; 1976.

The gross and microscopic pathology of hepatic cell cancer is reviewed, along with its routes of spread and differential diagnosis. Some commonly associated diseases such as cirrhosis, hemochromatosis, and hormonal abnormalities are also discussed. (123 refs.)

77-4868 **Cell Proliferation and Experimental Liver Cancer.** (Eng.) Craddock, V. M. (Medical Res. Council Toxicology Unit, Medical Res. Council Labs., Woodmansterne Road, Carshalton, Surrey SM5 4EF, England). *In: Liver Cell Cancer.* Cameron H. M.; Linsell, D. A.; Warwick, G. P., eds. (New York: Elsevier Scientific Publishing Co.): pp. 153-201; 1976.

The role of cell replication in the initiation of hepatic cell cancer is discussed. Hepatocarcinogens are capable of producing cancer in situations in which the cell proliferation rate is high, as in newborn animals or in adult animals undergoing restorative hyperplasia. The initiation of the carcinogenic process may result from the DNA replication that occurs before the damage from the carcinogen has been repaired by the cell. (277 refs.)

77-4869 **The Background to Liver Cell Cancer.** (Eng.) Anthony, P. P. (Bland Sutton Inst. Pathology, Middlesex Hosp., London W1N 8AA, England). *In: Liver Cell Cancer.* Cameron, H. M.; Linsell, D. A.; Warwick, G.

P., eds. (New York: Elsevier Publishing Co.) pp. 93-120; 1976.

Liver cell carcinoma has two outstanding features, its geographic distribution and its association in many cases with cirrhosis, whereas intrahepatic bile duct carcinoma has neither. The epidemiology and pathology of liver cell cancer are discussed, with particular attention to liver diseases that occur in areas where the tumor is common and to factors related to the cause of cirrhosis. (217 refs.)

77-4870 **The Geographic Pathology of Liver Cell Cancer.** (Eng.) Linsell, D. A. (International Agency Res. Cancer, 150 Cours Albert Thomas, 69372 Lyon, France); Higginson, J. *In: Liver Cell Cancer.* Cameron, H. M.; Linsell, D. A.; Warwick, G. P., eds. (New York: Elsevier Scientific Publishing Co.) pp. 1-16; 1976.

A study of the global frequency and types of liver cancer is presented. Discussion is made of the association of hepatic cancer with cirrhosis, especially the macronodular type, which is most often found in areas reporting a high incidence of liver cancer. Other etiologic factors such as environment, sex, and age are also reviewed. (87 refs.)

77-4871 **Geographical Pathology as a Method for Detecting Occupational Cancer.** (Eng) Goldsmith, J. R. (Epidemiological Studies Lab., California State Health Dept., CA). *J Occup Med* 19(8): 533-539; 1977.

The use of geographical pathology studies to suggest occupational carcinogen exposures is discussed. An occupational contribution has been established for cancer of the mouth, lung, bladder, skin, and penis, and, possibly, nasopharynx, brain, liver, pleura, nasal sinus, bone and bone marrow, lymphatic system, pancreas, and peritoneum. To define and corroborate the leads obtained from geographical variations in cancer mortality and morbidity, data from other sources, such as clinical observations, cancer registries and surveys, and from experimental studies are needed. Occupational cohort data are exceptionally useful. Preliminary geographical pathology studies have indicated a higher than expected mortality from lymphosarcoma in workers in the rubber and petroleum processing industries, in agricultural areas where arsenic-containing insecticides have been used, and in some coastal areas, possibly due to high levels of arsenic in shellfish. However, no definite and preventable occupational hazard has yet been defined. (18 refs.)

77-4872 **Epidemiology of Thyroid Cancer - Part I.** (Eng) Schottenfeld, D. (Epidemiology and Preventive Medicine Service, Dept. Medicine, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021); Gershman, S. T. *Clin Bull* 7(2): 47-54; 1977.

The incidence of thyroid cancer by age, sex, and race and its pathology are reviewed. A time trend analysis for age-adjusted mortality (1950-1967) indicates significantly decreasing mortality in white women and men but no significant trends for nonwhites. The female: male ratio of age-adjusted mortality rates is 2.0 in the white and 4.5 in the nonwhite US populations. New York State statistics indicate that, in cohorts born after 1910 and before 1949, there is a doubling of age-specific incidence with each successive decade of birth. The change in the cohort pattern after 1910 coincides with the administration of therapeutic x-rays to the neck in infancy and early childhood and is consistent with the hypothesis that ionizing radiation is a cause of thyroid cancer in children and young adults. There are striking differences in geographic and racial patterns for thyroid cancer incidence and mortality that should be studied carefully for differences in histopathology and natural history. The host and environmental factors that promote clinical expression of disease may be distinctive from those that initiate tumorigenesis. Most thyroid tumors arise from the epithelial elements of the gland and have been subdivided into papillary, occult sclerosing, follicular, Hurthle cell, medullary, and spindle and giant cell types. The prognosis for thyroid carcinoma patients correlates with histologic type, extent of disease, age at diagnosis, and sex. (29 refs.)

77-4873 **Carcinoma of the Esophagus.** (Eng) Gilder, S. S. (Cape Town, South Africa). *Ann Intern Med* 87(4): 494; 1977.

The incidence of esophageal carcinoma and the male:female ratio vary greatly from country to country and also within a particular country. The black male population appears to be particularly vulnerable. Epidemiologists have yet to find data that fit into a pattern. Since poor results are often obtained with therapy, epidemiological investigations of the disease are especially needed. (no refs.)

77-4874 **Australia's Needs in Cancer Epidemiology.** (Eng.) Donovan, J. (Epidemiology Section, Australian Dept. Health, P. O. Box 100, Curtin, ACT 2605, Australia). *Cancer Forum* (11): 408-410; 1977.

Cancer epidemiologists should have a more active part in the design of experiments and clinical trials so that the quality of data obtained will be improved. It is suggested that epidemiological research that is best carried out in Australia (eg, on cancers of the large bowel, rectum, and skin; various occupational cancers, and cancer in the aboriginals) be given priority. (no refs.)

77-4875 **Cancer Mortality of Hospitalized Psychiatric Patients.** (Fre.) Martin du Pan, R. (Clinique psychiatrique universitaire, Hopital de Cery, CH-1008 Prilly/Lausanne, Switzerland); Muller, C. *Schweiz Med Wochenschr* 107(17): 597-604; 1977.

The literature on cancer mortality in hospitalized psychiatric patients, especially schizophrenics, is reviewed. Differences in the results and conclusions of these studies may be partially explained by the various statistical, sampling, and diagnostic methods and observation times that were used. There is some evidence that cancer mortality may be lower in schizophrenics, but this may be due to the lower exposure of hospitalized psychiatric patients to tobacco, alcohol, diet high in protein and fat, and sexual activity. It has been suggested that tranquilizing neuroleptics have an antimitotic action; on the other hand, reserpine and the rauwolfia alkaloids have been implicated in breast cancer. Other theories related to carcinogenesis, such as immunological deficit and the cancer personality, are discussed in relation to mental patients. A biochemical defect is thought by some investigators to be responsible for schizophrenia and, simultaneously, for diminished cancer risk. On the whole, however, it is concluded that there is no major difference between cancer incidence in a nonselected population of psychotic patients (excluding psychoorganic patients) and the general population. (73 refs.)

77-4876 **Introduction: The Cancer Problem.** (Eng.) Nealon, T. F. (Dept. Surgery, St. Vincent's Hosp. and Medical Center New York, New York, NY) *In: Management of the Patient with Cancer.* Nealon, T. F., ed. (Philadelphia: W.B. Saunders Co.) pp. 3-11; 1977.

Recent changes in the incidence of cancers of various sites are summarized. Although the total number of cancer cases has increased, there have been decreases in some types of cancer and improved methods of treating others. Early diagnosis is emphasized. (no refs.)

77-4877 **A Statistician's Viewpoint of Familial Cancer.** (Eng.) Murphy, E. A. (Dept. Medicine, Johns Hopkins Univ. Sch. Medicine, Baltimore, MD 21205). *In: Genetics of Human Cancer.* Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F., eds. (New York: Raven Press): Progress in Cancer Research and Therapy Vol. 3, pp. 217-221; 1977.

Advice is directed at researchers who wish to know what statistical data should be reported from studies, and in how much detail. The distinction between moment and parameter in the developmental of biological hypotheses is discussed. The "sufficient statistic" is defined according to what is pertinent to a particular biologic model. (3 refs.)

77-4878 **A Chemical Approach to Cancer and Its Causes.** (Eng.) Anonymous (No affiliation given). *Manuf Chem Aerosol News* 48(6): 43, 44, 47; 1977.

Observations of cancer patients have led to the theory that two distinct groups of people exist, the acidic and the alkaline. Studies of these patients show that a lack of certain essential nutrients, as well as disturbances in the ratios of certain vitamins to certain minerals, may play a decisive role in the etiology of cancer. (no refs.)

77-4879 **Cancer and Vitamin K (Letter to Editor).** (Eng.) Hilgard, P. (Universitatsklinikum, Tumorforschung, S-4300 Essen 1, W. Germany) *Lancet* 2(8034): 403; 1977.

Experimental results indicate that a vitamin K deficiency is involved in the inhibition of tumor growth and dissemination in rodents. It is suggested that surface properties of the tumor cells are altered by impairment of vitamin K physiology. (8 refs.)

77-4880 **Some Therapeutic Implications of the Crosslinkage Theory of Aging.** (Eng.) Bjorksten, J. (Bjorksten Res. Foundation, Madison, WI 53715) *Adv Exp Med Biol* 86B: 579-602; 1977.

Several facts associating crosslinking and cancer are reviewed. DNA anomalies can be caused by crosslinkages, almost all known carcinogens are either themselves crosslinking agents or have metabolites that are, there is a high correlation between cytotoxicity and the ability to crosslink, and there is a correlation between carcinogenesis and exposure to known crosslinking agents. (98 refs.)

77-4881 **Effect of High-Oleic and High-Linoleic Safflower Oils on Mammary Tumors Induced in Rats by 7,12-Dimethylbenz(α)anthracene.** (Eng.) Dayton, S. (Res. Service, VA Wadsworth Hosp. Center, Los Angeles, CA 90024); Hashimoto, S.; Wollman, J. *J Nutr* 107(8): 1353-1360; 1977.

To test the hypothesis that polyunsaturated fatty acids are cocarcinogenic, oleic acid from a mutant strain of safflower oil (UC-1, which has oleic acid as its dominant fatty acid), linoleic acid from conventional safflower oil, or coconut oil was fed to weanling Sprague-Dawley rats treated with 7,12-dimethylbenz(α) anthracene (DMBA: 5 mg by gavage). The diets contained 20% by wt of oil. Under the conditions of the experiment, polyunsaturated fat was not cocarcinogenic. However, DMBA, regardless of the diet fed, produced a considerable diversity of lesions, which should be taken into account in future studies. There was no evidence that high-linoleic safflower oil was more cocarcinogenic than either of the other oils. (21 refs.)

77-4882 **Studies on the Effects of the Mammary Carcinogen 7,12-Dimethylbenz(a)anthracene on Release and Synthesis of Prolactin by Rat Pituitaries In Vitro.** (Eng) Ingleton, P. M. (Dept. Zoology, Univ., Western Bank, Sheffield S10, 2TN, England). *Eur J Cancer* 13(9): 1041-1048; 1977.

The effect of 7,12-dimethylbenz(a)anthracene (DMBA) on prolactin synthesis and release was investigated in female Wistar rats. Incubation of rat pituitaries with 50 μg/ml, 5 μg/ml or 0.5 μg/ml DMBA indicated a significant reduction in prolactin release with the first two concentrations but not with the third. DMBA effect was least at diestrus and max at proestrus. Experiments with male rats showed a similar response. The addition of 0.7 μg/ml haloperidol did not significantly increase prolactin release, indicating that DMBA was not acting by way of the dopamine receptor. Addition of 14.9 μg/ml phentolamine increased prolactin release, indicating that DMBA was acting through the α-andrenergic receptor; propranolol addition indicated that the carcinogen may also act through the β-andrenergic receptor. DMBA had no effect on growth hormone release, indicating a prolactin-specific interaction. With the addition of each of the various drugs alone (phentolamine, propranolol, ethanol, ascorbic acid, haloperidol, and DMBA) to the incubation media, there were no significant differences in prolactin content among any of the aliquots, including controls. DMBA inhibition of prolactin synthesis was not ameliorated by either phentolamine or propranolol, suggesting that inhibition of synthesis operates via a different mechanism than inhibition of release. (27 refs.)

77-4883 **Control of Hormone Receptor Levels and Growth of 7,12-Dimethylbenz(a)anthracene-induced Mammary Tumors by Estrogens, Progesterone and Prolactin.** (Eng) Asselin, J. (Medical Res. Council Group in Molecular Endocrinology, Le Centre Hospitalier de l'Universite Laval, Quebec G1V 4G2, Canada); Kelly, P. A.; Caron, M. G.; Labrie, F. *Endocrinology* 101(3): 666-671; 1977.

The effect of estradiol-17β (E_2), progesterone (P), and prolactin (PRL) treatment on hormone receptor levels in hormone-dependent 7,12-dimethylbenz(a)anthracene-induced tumors in female Sprague-Dawley rats was evaluated. 7,12-Dimethyl-19-norpregna-4,9,diene-3,20-dione (R5020) binding was also measured. The animals were inoculated sc daily for 3 wk with 0.5 μg E_2, 0.5 mg P, or 2 mg PRL or E_2 + PRL, E_2 + P, or a control solution. Ovariectomy led to a marked reduction in labeled E_2, R 5020, and ovine PRL binding in these tumors. Binding was reduced from 2.9 to 0.6 picomole (pmol)/g for E_2, 13.7 to 0.9 pmol/g for R 5020, and 3.2% to 0.9% for ovine PRL by 5.5 wk after ovariectomy. Treatment with P alone had no effect. Treatment with PRL alone caused a slight effect on PRL and no effect on R 5020 binding, but there was a significant stimulation of E_2 binding. Two tumors with high levels of E_2 binding had a max growth response to PRL. Addition of P or PRL to E_2 did not increase any levels. Treatment with P alone had no effect on tumor growth, whereas E_2 and PRL alone increased tumor size. Addition of P or PRL to E_2 increased tumor size to a greater extent than E_2 alone. (33 refs.)

77-4884 **Photosensitivity of DNA-bound 7,12-Dimethylbenz(a)anthracene.** (Eng.) Baird, W. M. (Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA 19104); Dipple, A. *Int J Cancer* 20(3): 427-431; 1977.

The photosensitivity of the products arising when 7,12-dimethylbenz(a)anthracene (DMBA) was bound to the DNA of Syrian hamster embryo cells in culture was examined. A comparison was made with the photosensitivities of various model compounds to determine which routes of metabolic activation might be involved in DMBA-DNA binding. Under light exposure conditions in which the DNA-DMBA products were highly photosensitive, 8,9,10,11-tetrahydro-DMBA and 5,6-dihydro-DMBA were stable. DMBA itself and the model compound 9,10-methylanthracene were also highly photosensitive. This suggests that DMBA is not bound to DNA through diol-oxide formation in the 8,9,10,11-ring. Also, the absence of photosensitivity in the 5,6-dihydro derivatives suggests that DMBA does not bind to DNA through a K-region oxide. In binding to DNA, DMBA either retains the aromatic benz(a)anthracene nucleus or is metabolically activated in the 1,2,3,4-ring. (18 refs.)

77-4885 **Photooxygenation of 7,12-Dimethylbenz(a)-anthracene.** (Eng.) Logani, M. K. (Skin and Cancer Hosp., 3322 N. Broad St., Temple Univ. Health Scineces Center, Philadelphia, PA 19140) Austin, W. A.; Davies, R. E. *Tetrahedron Lett* (29): 2467-2470; 1977.

Since studies of the effect of in vivo irradiation of polycyclic hydrocarbons on their carcinogenicity have given conflicting results, the in vitro photolysis of 7,12-dimethylbenz(a)anthracene (DMBA) was investigated in an attempt to determine the components of this interaction. The direct irradiation of a benzene solution of DMBA for 1 hr with a filtered xenon arc (295-400 nanometers) produced a novel bicyclic acetal of this hydrocarbon. It was separated and isolated by thin-layer chromatography. Its molecular formula, according to mass spectrometry, is $C_{20}H_{16}O_2$, indicating an addition of two oxygen atoms to DMBA. Unequivocal proof of the proposed structure for the acetal, which is included, was obtained by x-ray analysis. (8 refs.)

77-4886 **Clonal Behavior of a Rat Liver Cell Line and Its Modification by Repeated Treatments with a Carcinogenic Polycyclic Hydrocarbon.** (Eng) Starkey, J. R. (Dept. Veterinary Pathology, Washington State Univ., Pullman, WA 99164); Hosick, H. L. *J Natl Cancer Inst* 59(3): 859-866; 1977.

The results of treatment of Lew A_1 rat liver cells with 7,12-dimethylbenz[a]anthracene (DMBA) are presented. Normal karyotype and clonal behavior were first characterized. After the 9th passage and attainment of late log phase of growth cells were incubated with 1 μg/ml DMBA. After 2 days, the carcinogen was removed by washing. Cell death attributed to DMBA toxicity was noted soon after return of cultures to normal medium and continued for 1 wk to 10 days. DMBA treatment also increased the clonogenic percentage of the population; this percentage remained constant after each of three DMBA-induced increases and did not increase with further passages. Little DMBA toxicity was noted after second and third treatments. Large clones in excess of 400 cells/dish were noted only in the DMBA-treated cultures; increased pleomorphism was also noted in these cultures. Some of the cells treated with four applications of DMBA gave rise to colonies in soft agar, indicating a transformation frequency of about 0.005%. The reason for the increased clonogenic potential is unknown. (15 refs.)

77-4887 **Reaction of Arene Oxides with Nucleosides.** (Eng.) Friesel, H. (Institut fur Biochemie, Deutsches Krebsforschungszentrum, Heidelberg, W. Germany); Hecker, E. *Cancer Lett* 3(3-4): 169-175; 1977.

The alkylation of inosine and guanosine with the K-region epoxides of phenanthrene and 7,12-dimethylbenz(a)anthracene (DMBA) was studied to determine the molecular interaction of nucleic acids and polycyclic aromatic hydrocarbons (PAH) and the sites involved. Reaction of inosine with phenanthrene-9,10-oxide and DMBA-5,6-oxide yielded the corresponding N-1-alkylinosines. Reaction of guanosine with DMBA-5,6-oxide yielded a mixture of N-7-guanosines plus a smaller amount of an orcine-positive product whose UV spectrum resembles that of DMBA-5,6-dihydrodiol. When DMBA-5,6-oxide was reacted with either inosine or guanosine, a 5:1 mixture of positional isomers substituted at C_6 or C_5 resulted. (9 refs.)

77-4888 **Biosynthesis of Corticosterone and Deoxycorticosterone in Sprague-Dawley Male and Female Rats after Administration of 7,12-Dimethylbenzanthracene.** (Eng.) Carreau, S. (Department de Biochimie, C.H.U. Cote de Nacre, 14000, Caen, France); Joubert, F.; Chemama, A.; Drosdowsky, M. *J Steroid Biochem* 8(9): 971-976; 1977.

7,12-Dimethylbenzanthracene (DMBA, 20 mg/ml) was given to Sprague-Dawley rats of both sexes, and in vitro corticosterone biosynthesis, mitochondrial 11 β-hydroxylase activity, and cytochrome P-450 content were studied in the excised adrenal glands. Specimens from treated and untreated rats gave identical results, indicating that the rat adrenal cortex does not appear to be involved in DMBA induction of mammary tumors by secretion of corticosteroids. (17 refs.)

77-4889 **[G-^{3}H]-7,12-Dimethylbenz[a]anthracene 5,6-Oxide.** (Eng) Fu, P. P. (Ben May Lab. Cancer Res., Univ. Chicago, Chicago, IL 60637); Harvey, R. G. *J Labelled Compnd Radiopharm* 13(4): 619-621; 1977.

A method of synthesizing [G-^{3}H]-7,12-dimethylbenz-[a]anthracene 5,6-oxide (5,6-dihydro-7,12-dimethyl-5,6-epoxybenz[a]anthracene-G-^{3}H), a hydrocarbon metabolite with known mutagenic and carcinogenic activity, is presented. This technique should be applicable to the synthesis of other labeled K-region arene oxides. (9 refs.)

77-4890 **In Vitro Growth Characteristics of Epithelial Cell Lines Derived from Tracheal Transplants Exposed In Vivo to 7,12-Dimethylbenz(a)anthracene (DMBA) (Meeting Abstract).** (Eng.) Marchok, A. C. (Cancer and Toxicology Program, Oak Ridge Natl. Lab., Oak

Ridge, TN 37830); Nettesheim, P. *In Vitro* 13(3): 193; 1977. (no refs.)

77-4891 Cultivation of Human Adult Fibroblasts and an Attempt to Induce Malignant Transformation with 7,12-Dimethylbenz(a)anthracene (Meeting Abstract). (Eng) Kesava Rao, K. V. (Biology Division, Cancer Research Inst., Tata Memorial Centre, Parel, Bombay 400 012 India); Bhat, A. V.; Bapat, C. V. *In Vitro* 13(3): 184; 1977. (no refs.)

77-4892 Some Peculiarities Attending the Interaction of 9,10-Dimethyl-1,2-benzanthracene with the 'Hairy' Cells in the Central Nervous System of Rats. (Rus) Mardanova, G. V. (Inst. Human Morphology, USSR Acad. Medical Sciences, Moscow, USSR). ***Biull Eksp Biol Med*** 34(8): 197-199; 1977.

Implantation of a pill containing 1.5 to 2.0 mg dimethylbenz(a)anthracene into the right hemisphere of albino female SHK rat brain resulted in the formation of a capsule with hairy cells comprising the innermost layer. The carcinogen penetrated the hairy cell either by ordinary phagocytosis or as a result of biochemical interaction with the cell membrane. It is suggested that the latter results in secondary carcinogenic products in the form of steroid hormones which were identified as lipid-like structures in the cells. (15 refs.)

77-4893 An Animal Model for the Study of Prostatic Adenocarcinoma. (Eng) Fingerhut, B. (Columbia Univ., Coll. Physicians and Surgeons, Dept. Urology, New York, NY 10032); Veenema, R. J. *Invest Urol* 15(1): 42-48; 1977.

An attempt was made to induce prostatic adenocarcinoma in Fisher/Furth rats, Strong A/J mice, and golden hamsters. There were four groups of each species: normal animals; animals with prostate glands stimulated by transplantation of the pituitary gland into the subcapsular area of the kidney; animals with prostate glands stimulated by testosterone; animals inhibited by castration, with prostate glands atrophic. 9,10-Dimethyl-1,2-benzanthracene (DMBA) was administered iv (vena cava or jugular) to all animals once a mo for 3 mo beginning 1 mo after castration. The amount of 5-mg/ml DMBA emulsion administered per mo was 2 ml for rats, 0.5 ml for mice, and 1 ml for hamsters. All castrated animals that survived the experiment (11 rats, 22 mice, and 11 hamsters) developed prostate cancer in 3 to 4 mo. The histology of the neoplasm is described. Five mice, three rats, and one hamster developed metastasis to the lung similar to the prostatic adenocarcinoma. None of the other groups of animals developed tumors or had important changes in the histology of the prostate. (4 refs.)

77-4894 Expression of Alien H-2 Specificities on a Chemically Induced BALB/c Fibrosarcoma. (Eng) Meschini, A. (Div. Experimental Oncology A, Istituto Nazionale per lo Studio e la Cura dei Tumori, Via G Venezian I, 20133 Milan, Italy); Invernizzi, G.; Parmiani, G. *Int J Cancer* 20(2): 271-283; 1977.

Alien histocompatibility antigens on the surfaces of 3-methylcholanthrene (3-MC)-induced BALB/c (H-2d) fibrosarcoma C-1 cells were investigated by serological and transplantation studies. W/Fu rats were used along with the following strains of mice: inbred BALB/cLac/Dp (H-2d), C3Hf/He/Dp (H-2k), C57BL/6J/Dp (H-2b), AKR/Rd/Dp (H-2k), DBA/2/ChR (H-2d), A/He/N (H-2a), and N:NIH (S) (H-2q). Fibrosarcomas C-1, C-5, C-6, and TZ15 were induced in adult female BALB/c mice by sc application of Millipore disks containing 5% 3-MC. Fibrosarcoma ST2 originated from BALB/c fibroblasts exposed to 3-MC in a diffusion chamber placed ip in BALB/c mice. C-1 cells regularly absorbed both an anti-BALB/c polyspecific serum and antisera to H-2d private (K and D ends) and public specificities. This indicated that the neoplastic cells maintained most of their original BALB/c histocompatibility antigens, at least quantitatively. In experiments on the ability of C-1 cells to remove the cytotoxicity of H-2 monospecific sera directed against private and public specificities of haplotypes not expressed on normal BALB/c cells, C-1 lowered D-1 cytotoxicity by specifically absorbing the anti-1 antibodies. However, C-1 cells were unable to remove the activity of monospecific sera directed against D-32, D-33, D-2, D-17, and D-30. Cross-reaction tests among five different 3-MC-induced BALB/c tumors revealed common antigens between C-1 and ST2 but not among other sarcomas; furthermore, ST2 cells were unable to absorb monospecific anti-H-2k sera. An alloimmunization experiment suggested that the H-2.23, 1, 5, 11, and 25 specificities, alien to the C-1 cell, may be immunosensitive targets for in vivo antitumor transplantation resistance. BALB/c lymphocytes immune to C3Hf, AKR, and A tissues, but expressing these five alien specificites on C-1 cells, have a complete antitumor neutralizing effect. (41 refs.)

77-4895 Cell Surface Antigens of Chemically Induced Sarcomas of the Mouse. I. Murine Leukemia Virus-related Antigens and Alloantigens on Cultured Fibroblasts and Sarcoma Cells: Description of a Unique Antigen on BALB/c Meth A Sarcoma. (Eng) DeLeo, A. B. (Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021); Shiku, H.; Takahashi, T.; John, M.; Old, L. J. *J Exp Med* 146(3): 720-734; 1977.

Several fibroblast and sarcoma cell lines of BALB/c and C57BL/6 origin were typed by cytotoxicity and absorption tests for murine leukemia virus (MuLV)-related cell-surface antigens and known alloantigens. The cultured cell lines were assayed for MuLV expression by (1) microcytotoxicity tests with polyvalent anti-MuLV serum and with antiserum to MuLV structural components gp70 and p30, (2) by absorption tests for the two type-specific cell-surface antigens specified by MuLV (GIX) and Gross cell-surface antigen (GCSA), and (3) by XC assays for infectious MuLV ecotropic virus and assays for RNA-directed DNA polymerase (RDDP). Seven of the 17 cultured lines expressed the range of cell-surface antigens associated with MuLV, and this was always associated with MuLV production. In nonproducer lines of C57BL/6 (but not BALB/c) origin, a MuLV-gp70-like molecule was found on the surface of fibroblasts and sarcoma cells. A unique antigen was defined on the BALB/c ascites methylcholanthrene-induced sarcoma Meth A with antisera prepared in BALB/c or (BALB/c x C57BL/6)F_1 mice. Tissue culture lines derived from this tumor were MuLV, which facilitated serological study. Absorption analysis indicated that the antigen was restricted to Meth A; it could not be detected in normal or fetal BALB/c tissue, MuLV+, or MULV- fibroblast lines, 12 syngeneic or allogeneic sarcomas, or normal lymphoid cells from 13 different inbred mouse strains. (36 refs.)

77-4896 **Gene Expression in Chemically Transformed Mouse Embryo Cells: Selective Enhancement of the Expression of C Type RNA Tumor Virus Genes.** (Eng) Getz, M. J. (Dept. Pathology, Mayo Clinic and Mayo Foundation, Rochester, MN 55901); Reiman, H. M.; Siegal, G. P.; Quinlan, T. J.; Proper, J.; Elder, P. K.; Moses, H. L. *Cell* 11(4): 909-921; 1977.

The expression of poly(a)-containing messenger RNA (mRNA) sequences in AKR mouse embryo cells transformed by 3-methylcholanthrene (3-MC, 1 μg/ml for 7 days) was compared with that of the parent clone (2B). The poly(A)-containing sequences of both clones were found to be organized into indistinguishable abundance classes, and the majority of the sequences were common to both clones. The levels of α- and β-globin mRNA that characterize highly differentiated mouse erythroid cells were less than one molecule per cell in either cell type. Approx 5,000 and 1,200 AKR murine leukemia virus 35S RNA equivalents were present in the cytoplasm of growing and resting 3-MC transformed cells, respectively. Rapidly growing 2B cells contained $<$ 30 viral 35S RNA equivalents per cell. Virus specific sequences thus occur in the high-abundance class of poly(A)-containing RNA sequences in MC-transformed cells and in the low-abundance class in 2B cells. Within the limits of detection, this large increase is characteristic only of virus specific RNA sequences. (43 refs.)

77-4897 **3-Methylcholanthrene Inducibility of Aryl Hydrocarbon Hydroxylase in Cultured Human Lymphocytes Depends upon the Extent of Blast Transformation.** (Eng.) Hart, P. (Dept. Medicine and Biochemistry, Univ. Queensland, Royal Brisbane Hosp., Brisbane, 4029, Australia); Cooksley, W. G.; Farrell, G. C.; Powell, L. W. *Biochem Pharmacol* 26(19): 1831-1834; 1977.

Evidence is presented that the extent of induction of aryl hydrocarbon hydroxylase (AHH), as measured in lymphocyte culture, varies with the length of culture and is directly dependent upon the blastogenic state of the cells at harvest. 3-Methylcholanthrene (MC)-induced AHH activity was followed at daily intervals over a period of 2 to 7 days in cultures of lymphocytes from four normal healthy men 29-35 yr old. Control AHH activity in the cells varied little with increased time in culture, but MC-induced AHH activity increased sharply to a max. This max occurred after widely variable times in culture for lymphocytes from each individual. It coincided with the time of max DNA synthesis. Variation in the degree of blast transformation was reflected by variation in the extent of induced AHH activity for each individual. Thus, induction of AHH by MC in cultured human lymphocytes depends largely on the degree of blast transformation of the cells at harvest. (8 refs.)

77-4898 **Variability of Physiological and Karyotypic Characteristics of BALB/c-3T3 Cell Populations (Meeting Abstract).** (Eng) Sivak, A. (Arthur D. Little, Inc., Cambridge, MA 02140); Rudenko, L.; Simons, I. *In Vitro* 13(3): 198-199; 1977. (no refs.)

77-4899 **The Metabolism of Benzo(a)pyrene in Isolated Perfused Lungs from Variously-treated Rats.** (Eng) Vahakangas, K. (Dept. Pharmacology, Univ. Oulu, SF-90220 Oulu 22, Finland); Nevasaari, K.; Pelkonen, O.; Karki, N. T. *Acta Pharmacol Toxicol* 41(2): 129-140; 1977.

The metabolism of benzo(a)pyrene (BP) was studied during short- and long-term perfusion of isolated rat lung. Male Sprague-Dawley rats were pretreated by ip injection of 40 mg/kg 3-methylcholanthrene (3-MC) for 3 days, by 0.5 g/liter phenobarbitone (PB) in the drinking water for 7 days, or by three exposures to cigarette smoke during the 2 days before perfusion. The half-life of BP was 15 min in the perfusions of lungs from 3-MC-treated rats and 60-90 min in those from PB-treated and control rats. The appearance of water-soluble metabolites was rapid and marked in the perfusions of lungs from 3-MC rats, at 15 min being 2.5 times and at 2 hr twice that seen for controls. Phenols were the most prominent organic solvent-soluble metabolites at the beginning of perfusion in 3-MC rats. The covalent binding of radioactivity in the 3-MC rat lungs was 3.5 times higher than that in control and PB rat lungs. There was a positive correlation between the amount of radioactivity bound covalently and BP hydroxylase activity in the lung homogenates. Exposure of the rats to cigarette smoke gave results similar to those of 3-MC pretreatment. The isolated perfused rat lung may be valuable for studying the metabolism of polycyclic hydrocarbon carcinogens in their target organ, without the influence of the rest of the body. (20 refs.)

77-4900 **Temporal Acquisition of Enhanced Fibrinolytic Activity by Syrian Hamster Embryo Cells Following Treatment with Benzo(a)pyrene.** (Eng) Barrett, J. C. (Natl. Inst. Environmental Health Sciences, Post Office Box 12233, Research Triangle Park, NC 27709); Crawford, B. D.; Grady, D. L.; Hester, L. D.; Jones, P. A.; Benedict, W. F.; Ts'O, P. O. *Cancer Res* 37(10): 3815-3823; 1977.

The time required for the expression of enhanced fibrinolytic activity in benzo(a)pyrene-treated Syrian hamster embryo cells was examined. A fibrin-agarose overlay method was used to distinguish the activity of normal and transformed colonies. Colonies possessing enhanced fibrinolytic activity were not observed 8 days after treatment, but they were observed following one passage (2 wk after treatment). Morphologically transformed colonies, which exhibited no enhanced fibrinolytic activity, were observed 8 days following treatment. In contrast to these two early changes, cells capable of growth in soft agar were not observed until 6 to 8 wk after treatment. Untreated Syrian hamster embryo cells generally senesced and did not exhibit enhanced fibrinolytic activity. Approx 1/10 untreated cultures escaped senescence and evolved as a continuous cell line; these cultures frequently exhibited enhanced fibrinolytic activity. These results suggest that the acquisition of enhanced fibrinolytic activity may reflect a loss of control of the normal function of the cellular genetic apparatus during transformation. (40 refs.)

77-4901 **Fluorescence Cytochemical Study of the Action of Benzo(a)pyrene on Subcutaneous Connective Tissue Cells During In Vitro Malignant Transformation.** (Rus) Ruchkovskii, B. S. (Dept. Environmental Carcinogens, Inst. Oncological Problems, Acad. Sciences Ukranian SSR, Kiev, USSR); Antonenko, S. V. *Tsitologiia* 19(8): 937-939; 1977.

The in vitro effect of benzo(a)pyrene (BP) on rat sc tissue was investigated using the Roshlay fluorescent-cytochemical method. The greatest changes in the secondary structure of the DNA were noted after injection of the carcinogen on the third day of culture. Repeated injections on the 10th and 20th days resulted in fewer toxic effects. Cells malignantly transformed by BP became more resistant to BP's toxic action than normal cells; cells that spontaneously underwent transformation were also more sensitive to BP toxicity than BP-transformed cells. (8 refs.)

77-4902 **Changes in Phospholipid Composition in Rat Liver Microsomes and Mitochondria under Chemical Carcinogenesis.** (Rus) Poliakov, V. M. (Rostov Scientific Res. Inst. Oncology, Ministry Public Health RSFSR, Rostov, USSR); Lankin, V. Z. *Biokhimiia* 42(5): 799-808; 1977.

Changes in the phospholipid composition of microsomal and mitochondrial liver membranes in random-bred male albino rats were investigated following a single sc dose of 5 mg 3,4-benzo(a)pyrene. Phosphatidylethanolamines and phosphatidylcholines in liver microsomes increased in the precancerous stage and decreased during tumor growth. On the other hand, phospholipid content in mitochondria decreased during the precancerous stage and increased during vigorous tumor growth. Phosphatidylserines in microsomes sharply increased during tumor growth while mitochondrial levels decreased beginning in early carcinogenesis. Lysophosphatide content in microsomes increased during carcinogenesis. Microsomal phospholipids and sphingomyelins appeared in noticeable amounts in mitochondria during tumor growth. Phosphatidylethanolamine peroxides and phosphatidylcholine epoxides were noted at later stages of carcinogenesis in mitochondria, as compared to microsomes. (24 refs.)

77-4903 **Binding of 6-Oxybenzo(α)pyrene Radical with DNA and Polynucleotides.** (Eng.) Kodama, M. (Biophysics Div., Natl. Cancer Center Res. Inst., Tsukiji 5-1-1, Chuo-ku, Tokyo 104, Japan); Nagata, C. *Gann* 68(1): 125-126; 1977.

Experimental data strongly suggest the participation of the 6-oxybenzo(α)pyrene radical in DNA binding. Recent findings of high mutagenicity of 6-hydroxybenzo(α)pyrene in *Salmonella typhimurium* strain TA98 and in Chinese hamster cells without enzymatic activation further support the biological importance of metabolism at position 6 in benzo(α)pyrene. (4 refs.)

77-4904 **Skin-Tumor-initiating Ability of Benzo(a)pyrene-7,8-diol-9,10-epoxide (Anti) When Applied Topically in Tetrahydrofuran.** (Eng.) Slaga, T. J. (Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830) Viaje, A.; Bracken, W. M.; Berry, D. L.; Fischer, S. M.; Miller, D. R.; LeClerc, S. M. *Cancer Lett* 3(1/2): 23-30; 1977.

The skin tumor-initiating abilities of various metabolites of benzo(a)pyrene (BP) were determined in female CD-1 mice by a two-stage system of tumorigenesis. Because of its high reactivity, the tumor-initiating ability of BP 7,8-dihydrodiol-9,10-epoxide (anti), the alleged ultimate carcinogen of BP, was determined by using acetone, benzene, and tetrahydrofuran (THF) as the solvent vehicles. The diol epoxide of BP was an effective tumor initiator when applied topically in THF. The effectiveness of the various vehicles for the diol epoxide was THF > benzene > acetone; however, acetone was the best solvent for BP tumor initiation. BP-9,10-dihydrodiol and BP-3-hydroxy were weak tumor initiators. In addition, BP-3-hydroxy was inactive as a tumor promoter. (32 refs.)

77-4905 **The Metabolism of Benzo(a)pyrene, 7,8-Dihydro-7,8-dihydroxybenzo(a)pyrene and 9,10-Dihydro-9,10-dihydroxybenzo(a)pyrene by Short-Term Organ Cultures of Hamster Lung.** (Eng.) Cohen, G. M. (Dept. Biochemistry, Univ. Surrey, Guildford, GU2 5XH, Surrey, England); Moore, B. P. *Biochem Pharmacol* 26(16): 1481-1487; 1977.

The metabolism of benzo(a)pyrene (BP) and two of its metabolites, 9,10-dihydro-9,10-dihydroxybenzo(a)pyrene (9,10-dihydrodiol) and 7,8-dihydro-7,8-dihydroxybenzo-(a)pyrene (7,8-dihydrodiol) by short-term organ cultures of hamster lung to both ethyl acetate-soluble and water-soluble metabolites is described. The 7,8- and 9,10-dihydrodiols are further metabolized to 7,8,9,10-tetrahydro-7,8,9,10-tetrahydroxybenzo(a)pyrene (7,8,9,10-tetrahydrotetrol). BP was metabolized by short-term organ culture to ethyl acetate-soluble metabolites that cochromatographed with 9,10- and 7,8-dihydrodiols and BP-3-yl hydrogen sulfate. Significant amounts of the 7,8-dihydrodiol but not 9,10-dihydrodiol were converted into water-soluble conjugates. This agreed with several previous observations showing the high biological activity of the further metabolite of 7,8-dihydrodiol, 7,8-dihydro-7,8-dihydroxybenzo(a)pyrene 9,10-oxide. The results also raise the possibility of a role for 9,10-dihydrodiol as a precursor of active metabolites. (27 refs.)

77-4906 **Evidence for a 2,3-Epoxide as an Intermediate in the Microsomal Metabolism of Benzo(a)pyrene to 3-Hydroxybenzo(a)pyrene.** (Eng) Yang, S. K. (Dept. Pharmacology, Uniformed Services Univ. Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20014); Roller, P. P.; Fu, P. P.; Harvey, R. G.; Gelboin, H. V. *Biochem Biophys Res Commun* 77(4): 1176-1182; 1977.

A synthetic benzo(a)pyrene (BP) specifically labeled with ^{3}H at the 3-position was incubated with rat liver microsomes in the presence of NADPH and oxygen to study the enzymatic formation of 3-hydroxybenzo(a)pyrene (3-OH-BP). If 3-OH-BP is formed by direct hydroxylation of ^{3}H-BP, there would be no retention of ^{3}H label. Retention of a detectable amount of label in the enzymatically formed 3-OH-BP would indicate that a 2,3-epoxide is an obligatory intermediate. Mass spectral analysis of the metabolites isolated by high-pressure liquid chromatography indicated that 3-OH-BP and BP-3,6-quinone retained 29% and 15% of the label, respectively, but the BP trans 4,5 -7,8-, and 9,10-diols, 9-OH-BP, BP-1,6-quinone, and BP-6,12-quinone retained essentially all the label. These results indicate that at least 29% of the 3-OH-BP detected as a metabolite is formed through a 2,3-epoxide intermediate that rearranges spontaneously via an NIH shift mechanism to 3-OH-BP. At least 15% of the BP-3,6-quinone detected as a metabolite is derived from the enzymatically formed 3-OH-BP. (29 refs.)

77-4907 **Carcinogenicity of Benzo-Ring Derivatives of Benzo(a)pyrene on Mouse Skin.** (Eng) Levin, W. (Dept. Biochemistry and Drug Metabolism, Hoffmann-LaRoche, Inc., Nutley, NJ 07710); Wood, A. W.; Wislocki, P. G.; Kapitulnik, J.; Yagi, H.; Jerina, D. M.; Conney, A. H. *Cancer Res* 37(9): 3356-3361; 1977.

Several benzo-ring derivatives of benzo(a)pyrene (BP) were tested for their carcinogenicity on mouse skin. Topical application of 0.10 micromole (μmol) of BP to C57BL/6J mice once every 2 wk for 60 wk resulted in a tumor incidence of 38%; a dose of 0.4 μmol produced a 100% incidence. Chronic application of (±)-trans-7,8-dihydroxy-7,8-dihydro-BP (7,8-dihydrodiol) was even more potent: doses of 0.025, 0.05, and 0.10 μmol produced tumors in 22%, 76%, and 92% of the mice, respectively. 7,8-Dihydroxy-7,8,9,10-tetrahydro-BP, which is related to the 7,8-dihydrodiol but lacks the double bond at position 9,10, was inactive. Thus, the double bond at position 9,10 is important for the carcinogenicity of the 7,8-dihydrodiol. Chronic application of 0.4 μmol of (±)-$7\beta,8\alpha$-dihydroxy-9α, 10α-epoxy-7,8,9,10-tetrahydro-BP, (a potent mutagen), (±)-$7\beta,8\alpha$-dihydroxy-$9\beta,10\beta$-epoxy-7,8,9,10- tetrahydro-BP, or 9,10-epoxy-7,8,9,10-tetrahydro-BP resulted in tumor incidences of 0%, 8%, and 4%, respectively. The high reactivity of these three epoxides may account for their inactivity or weak carcinogenicity on mouse skin. (27 refs.)

77-4908 **In Vitro Reactions of the Diastereomeric 9,10-Epoxides of (+) and (-)-trans-7,8-Dihydroxy-7,8-dihydrobenzo(a)pyrene with Polyguanylic Acid and Evidence for Formation of an Enantiomer of Each Diastereomeric 9,10-Epoxide from Benzo(a)pyrene in Mouse Skin.** (Eng) Moore, P. D. (Dept. Chemistry, Johns Hopkins Univ., Baltimore, MD 21218); Koreeda, M.; Wislocki, P. G.; Levin, W.; Conney, A. H.; Yagi, H.; Jerina, D. M. *In: Drug Metabolism Concepts.* Jerina, D. M., ed. (Washington, DC: American Chemical Society): ACS Symposium Series 44, pp. 127-154; 1977.

The in vitro reactions of the diastereomeric 9,10-epoxides of (+)- and (-)-trans-7,8-dihydroxy-7,8-dihydrobenzo(a)pyrene (cis, designated diol epoxide 1, and trans, designated diol epoxide 2) with polyguanylic acid [poly(G)] were studied, and the structure of the RNA adducts that form when ^{3}H-benzo(a)pyrene (BP) is painted on mouse skin was determined. Both diol epoxides 1 and 2 reacted similarly with poly(G) in 50% acetone/water. Alkylation occurred at phosphate sites (10%-15%) and at the exocyclic 2-amino group of guanosine. This reactivity under neutral conditions was also demonstrated by alkylation of inorganic phosphate. Mice were painted with ^{3}H-BP, and the isolated RNA was hydrolyzed to a mixture of nucleosides. Adducts from diol epoxides 1 and 2 were identified. These adducts are optically active, and their absolute stereochemistry was assigned through the use of the optically pure enantiomers of diol epoxides 1 and 2. The results indicate that the monooxygenases in mouse skin that produce the 9,10-epoxides are highly stereoselective, in that (+)-diol epoxide 1 from (+)-BP 7,8-dihydrodiol and (+)-diol epoxide 2 from (-)-BP 7,8-dihydrodiol formed, predominantly, detectable RNA adducts. Whether or not the enantiomers of diol epoxides 1 and 2 are important in the binding of BP to the DNA of mouse skin is under study. (64 refs.)

77-4909 **Role of Purified Cytochrome P-448 and Epoxide Hydrase in the Activation and Detoxification of Benzo(a)pyrene.** (Eng) Levin, W. (Dept. Biochemistry and Drug Metabolism, Hoffmann-La Roche Incorporated, Nutley, NJ 07110); Wood, A. W.; Lu, A. Y.; Ryan, D.; West, S.; Conney, A. H.; Thakker, D. R.; Yagi, H.; Jerina, D. M. *In: Drug Metabolism Concepts.* Jerina, D. M., ed. (Washington, DC: American Chemical Society): ACS Symposium Series. 44, pp. 99-126; 1977.

Studies to identify the ultimate mutagenic and carcinogenic metabolites of benzo(a)pyrene are reviewed. A procedure using the purified monoxygenase system and epoxide hydrase (EH) was developed to help clarify the ultimate mutagenic metabolites(s) of BP. In the absence of EH, the cytochrome P-448-containing purified monoxygenase system metabolized BP to arene oxides, phenols, and quinones. Of 21 known and potential primary oxidative metabolites of BP that have been tested for mutagenicity in the *Salmonella typhimurium* assay, only BP 4,5-oxide is a potent mutagen. This indicates that BP 4,5-oxide probably accounts for most of the mutations induced when BP is metabolically activated by the monoxygenase system in the absence of EH. Addition of EH to the monoxygenase system decreased mutations in *S. typhimurium* strain TA98 by 30%. The mutations observed when BP was metabolically activated in the presence of EH were not due to BP 4,5-oxide, because EH completely inactivates BP 4,5-oxide as a bacterial mutagen. Addition of EH to the monoxygenase system, however, results in the formation of BP 7,8-dihydrodiol, which is metabolically activated to the highly mutagenic stereoisomeric BP 7,8-diol-9,10-epoxides, which are not substrates for EH. The effect of EH on the metabolic activation of BP to mutagenic metabolites appears, therefore, to be a composite of the inactivation of BP 4,5-oxide and the activation of BP 7,8-oxide via BP 7,8-dihydrodiol to BP 7,8-diol-9,10-epoxide. (49 refs.)

77-4910 **Genetic Difference in the Metabolism of Carcinogens and in the Binding of Benzo(a)pyrene Metabolites to DNA.** (Eng) Boobis, A. R. (Developmental Pharmacology Branch, Natl. Inst. Child Health and Human Development, NIH, Bethesda, MD 20014); Nebert, D. W. *Adv Enzyme Regul* 15: 339-362; 1977.

C3H, C57BL/6, and DBA/2 mice were used to study the relationship between benzo(a)pyrene (BP)-initiated tumorigenesis in vivo and nucleoside BP metabolites generated in vitro. Numerous conditions in the mouse, including an increased susceptibility to chemical carcinogenesis and drug toxicity, are associated with the *Ah* locus--a single gene or a small number of genes. The various forms of cytochrome P-450 in mouse liver or skin microsomes produce reactive metabolites of BP that bind to DNA in vitro. Nine peaks, reflecting BP metabolites bound to DNA nucleosides, can be reproducibly identified from C3H, C57BL/6, and DBA/2 mice. When the C3H or C57BL/6 strain is compared with the DBA/2 strain, a positive correlation is found between carcinogenic index in vivo and each of three determinations in vitro: the size of 8/9 peaks, hepatic aryl hydrocarbon hydroxylase activity, and total hepatic cytochrome P-450 content. Four peaks (D,E,H,I) show relative differences among the three strains that are in the same direction as the carcinogenic index in vivo; ie, the peaks are greater in C3H than in C57BL/6 mice and the peaks in both are much greater than those in DBA/2 mice. When C3H mice are compared with C57BL/6 mice, however, no quantitative correlation is found between the carcinogenic index and any of the three determinations. Hence, the total quantity of nucleoside BP metabolites in each of the nine peaks is not necessarily associated with BP carcinogenicity in vivo. Cultured human lymphocytes and microsomes from a human liver biopsy were capable of metabolizing BP to intermediates that bind to DNA and cause peaks similar to those found with mouse liver or skin microsomes. (77 refs.)

77-4911 **In Vitro Metabolic Activation Systems (Meeting Abstract).** (Eng) Kouri, R. E. (Dept. Biochemical Oncology, Microbiological Assoc., Bethesda, MD 20014); Schechtman, L. M. *In Vitro* 13(3): 192; 1977. (no refs.)

77-4912 **Relationship of Aryl Hydrocarbon Hydroxylase Activity to Benzo(a)pyrene-metabolizing Activity of Cells in Culture.** (Eng.) Diamond, L. (Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA 19104); Baird, W. M. *Cancer Lett* 3(3-4): 189-195; 1977.

The relationship between aryl hydrocarbon hydroxylase

(AHH) inducibility and the actual hydrocarbon-metabolizing capacity of a cell was investigated. Two cell lines that differed widely in inducibility were selected, and their capacity to metabolize benzo(a)pyrene (BP) was compared. Primary Syrian hamster embryo (HE) cells, and R72/3 cells derived from a tumor produced by rat liver cells that had transformed spontaneously in culture were used. The basal level of AHH activity was high in HE cells but AHH inducibility by benzo(a)anthracene (BA) was low; in R72/3 cells, the basal activity was low and inducibility was high. Although HE cells had low and R72/3 cells had high AHH inducibility, the metabolism of BP in uninduced and BA-induced HE cells and BA-induced R72/3 cells was similar. This suggests that the untreated HE cells were expressing essentially their max BP-metabolizing capacity. The absolute levels of induced AHH are a measure of cell hydrocarbon-metabolizing capacity, but the absolute levels of uninduced AHH are a measure of their initial metabolizing activity after exposure to the hydrocarbon. However, inducibility need not correspond to the cells' max hydrocarbon-metabolizing capacity. (11 refs.)

77-4913 **Induction of Aryl Hydrocarbon Hydroxylase and Forestomach Tumors by Benzo(a)pyrene.** (Eng.) Triolo, A. J. (Dept. Pharmacology, Jefferson Medical Coll., Thomas Jefferson Univ., 1020 Locust St., Philadelphia, PA 19107); Aponte, G. E.; Herr, D. L. *Cancer Res* 37(9): 3018-3021; 1977.

The relationship between the inducibility of aryl hydrocarbon hydroxylase (AHH) in various Ha-ICR mouse tissues, including two portions of the stomach (forestomach vs glandular), and the induction of forestomach tumors by benzo(a)pyrene (BP) was studied. The forestomach was susceptible to papillomatous tumor development after a 12-wk period of feeding BP (0.2 or 0.3 mg/g diet). The glandular stomach did not form tumors and thus is apparently resistant to the carcinogenic action of BP. The mechanism by which squamous cells of the forestomach give rise to papillomatous tumors by feeding BP is not known. The basal level of AHH was higher in the forestomach than in the glandular stomach. It is generally believed that BP must be metabolically activated by the AHH enzyme system to form reactive carcinogenic epoxides. (28 refs.)

77-4914 **Induction of Aryl Hydrocarbon (Benzo[a]Pyrene) Hydroxylase and 2-Acetylaminofluorene N-Hydroxylase by Polycyclic Hydrocarbons in Regenerating Liver from Inbred Strains of Mice.** (Eng.) Boobis, A. R. (Lab. Chemical Pharmacology, NCI, NIH, Bethesda, MD 20014); Reinhold, C.; Thorgeirsson, S. S. *Biochem Pharmacol* 26(16): 1501-1505; 1977.

Evidence is given that partial hepatectomy neither affects the max 3-methylcholanthrene (MC)-induced (80 mg/kg ip) activities of aryl hydrocarbon hydroxylase (AHH) and 2-acetylaminofluorene N-hydroxylase in responsive C57BL/6N mice nor increases these enzyme activities after MC treatment in nonresponsive DBA/2N mice. Both basal and MC-induced AHH and N-hydroxylase activities were reduced 70% within 12 hr after partial hepatectomy in C57BL/6N mice, but levels returned to control values between 36 and 48 hr. Similar but less pronounced changes (20% reduction) were observed in DBA/2N mice. Despite the decrease in basal AHH activity after partial hepatectomy in C57BL/6N mice, MC induction became apparent in these mice 12 hr after it was injected. Neither AHH nor N-hydroxylase were induced by MC in the regenerating liver from DBA/2N mice, indicating that even during periods of rapid cell growth the genetic expression of these enzyme activities is similar to that in the intact liver. Replicating cells may be especially vulnerable to the action of carcinogens. (16 refs.)

77-4915 **Benzo(a)pyrene Metabolism in Mouse Epidermis. Analysis by High Pressure Liquid Chromatography and DNA Binding.** (Eng) Berry, D. L. (Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830); Bracken, W. R.; Slaga, T. J.; Wilson, N. M.; Butty, S. G.; Juchau, M. R. *Chem Biol Interact* 18(2): 129-142; 1977.

The effects of 5,6-benzoflavone (5,6-BF), 7,8-benzoflavone (7,8-BF), butylated hydroxytoluene (BHT), 17β-estradiol, and 1,2-epoxy-3,3,3-trichloropropane (TCPO) on the covalent binding of polycyclic aromatic hydrocarbons (PAH) in vitro was investigated. The metabolism of benzo(a)pyrene (BP) by epidermal homogenates of female Charles River CD-1 mice and epidermal epoxide hydratase activity were also investigated using BP-4,5-oxide as substrate. The mice were topically treated with 3-methylcholanthrene (MC) 18 hr prior to killing. High-pressure liquid chromatography revealed that the major products of BP metabolism were 3-OH-BP and 9-OH-BP; upon 3-MC treatment, the epidermal homogenates metabolized BP to the preceding two compounds plus BP-1,6-quinone, BP-7,8-diol and several compounds with greater polarity than BP-7,8-diol. The rates of formation of the major metabolites in the 3-MC treated animals increased at an approx linear rate for up to 60 min; formation rates in controls were low compared to those in 3-MC treated mice. The rates of metabolite formation increased with increasing protein concentration, but this was not true for the minor protein metabolites. The addition of BHT almost doubled the total BP metabolism and increased production of phenols, quinones, and BP-7,8-diol. 7,8-BF and 5,6-BF decreased the formation of diols, quinones and phenols. 17β-Estradiol and TCPO decreased total BP metabolism by 80% and 40%, respectively. 5,6-BF and 7,8-BF inhibited the homogenate-mediated binding of BP to DNA; BHT and TCPO had no significant effect. Pretreatment with BP 18 hr before killing almost doubled the DNA binding, as compared to controls. (41 refs.)

77-4916 **Sex-dependent Regulation of Benzo(a)pyrene and Zoxazolamine Metabolism in Rat Tissues.** (Eng) Gurtoo, H. L. (Dept. Experimental Therapeutics, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263); Parker, N. B. *Drug Metab Dispos* 5(5): 474-481; 1977.

The hepatic microsome-catalyzed metabolisms of benzo(a)-pyrene (BP) to phenols, measured by the fluorometric aryl hydrocarbon hydroxylase (AHH) assay, and to reactive metabolites, measured by the formation of DNA-binding metabolites of BP (metabolic activation), were studied in male and female rats of five strains. In addition to these activities, hydroxylation of zoxazolamine was measured in hepatic microsomes isolated from normal and gonadectomized male and female rats and from testosterone-treated castrated males and normal females. Hepatic AHH activity of normal and gonadectomized male and female rats was compared with that in kidney, lung, and spleen. Castration decreased BP metabolism by about 50%, whereas ovariectomy had no effect on its metabolism. Testosterone treatment of castrated, immature males and immature females enhanced BP metabolism. Although all the activities tested showed a sex difference, the difference was the greatest for AHH activity (four to sixfold) and the lowest for zoxazolamine hydroxylase activity (about 40%); it was about 50% for the metabolic activation of BP. The sex difference in AHH activity was seen in all rat strains tested. The hepatic activity of AHH was the lowest in both sexes of Wistar rats. No sex differences in lung or spleen AHH activity were discernible, but AHH activity of the female rat kidney was about 80% greater than that of the male kidney. These data suggest that in the rat, sex-dependent regulation of microsomal mixed-function oxygenase activity is organ-specific. (56 refs.)

77-4917 **The Use of Primary Rat Liver Parenchymal Cells in Evaluating Cellular Response to Toxic Metals and Carcinogenic Polycyclic Aromatic Hydrocarbons (Meeting Abstract).** (Eng) Huisingh, J. L. (Environmental Protection Agency, Health Effects Res. Lab., Research Triangle Park, NC 27711); Inmon, J. P.; King, L. C.; Williams, K.; Waters, M. D. *In Vitro* 13(3): 182; 1977. (no refs.)

77-4918 **Biliary Excretion of Cadmium in the Rat, Rabbit, and Dog.** (Eng.) Klaassen, C. D. (Dept. Pharmacology, Univ. Kansas Medical Center, Coll. Health Sciences and Hosp., Kansas City, KS 66103) Kotsonis, F. N. *Toxicol Appl Pharmacol* 41(1): 101-112; 1977.

The biliary excretion of cadmium was investigated in Sprague-Dawley rats, New Zealand white rabbits, and mongrel dogs. Biliary excretion was shown to be the main route for elimination; the rate was dependent on the time after administration, dose, and species. Phenobarbital increased the excretion. (28 refs.)

77-4919 **Carcinogen Delivery into the Pancreatic Duct of Rabbits by Means of Hollow Fiber Capsules.** (Eng) Elkort, R. J. (Univ. Hosp., 75 E. Newton St., Boston, MA 02118); Handler, A. H.; Cooper, W.; Williams, D. L.; Mozden, P. J.; Egdahl, R. H. *World J Surg* 1(2): 259-266; 1977.

A technique was developed for the delivery of chemical agents chronically and in small doses into the rabbit pancreatic duct, and it was used to determine the effectiveness of benzo(a)pyrene (BP) and methylnitrosourethane (MNU) as pancreatic carcinogens. A catheter permeation system using a silicone membrane was designed so that it can be anchored in the main pancreatic duct without ligating it. The ductal cells can then be continuously exposed to chemical carcinogens over a 5- to 30-day period. The catheters were loaded with 10 μl of dissolved carcinogen before implantation. Exposure of New Zealand white rabbit ductal cells to BP produced slowly progressive hyperplasia, dysplasia, and adenosis up to 62 wk after implantation. MNU exposure produced a primary inflammatory response that resulted in progressive acinar atrophy. Although evidence of acinar regeneration associated with ductal cell hyperplasia and dysplasia was seen between 43 and 64 wk after implantation of the MNU catheter, much of this activity probably represents a response to inflammation rather than a direct carcinogenic response. It is possible that the BP changes are preneoplastic, since similar changes were not observed in control animals. This study supports the premise that sustained growth stimulation may be a prerequisite for chemical carcinogenesis. (3 refs.)

77-4920 **The Binding of Benzo(a)pyrene and N-Methyl-N′-nitro-N-nitrosoguanidine to Subnuclear Fractions of AKR Mouse Embryo Cells in Culture.** (Eng) Zytkovicz, T. H. (Dept. Molecular Medicine, Mayo Clinic, Rochester, MN 55901); Moses, H. L.; Spelsberg, T. C. *Int J Cancer* 20(3): 408-417; 1977.

The binding of benzo(a)pyrene (BP) and N-methyl-N′-nitro-N-nitrosoguanidine (MNNG) to a specific subnuclear fraction (I) from AKR-2B mouse embryo cells in culture is described. Fraction I was isolated by sucrose gradient centrifugation of sheared nuclei from exposed cells. There were two types of binding of ^{3}H-BP to fraction I: a weak binding representing the radioactivity that can be extracted by organic solvents and a covalent binding representing the radioactivity that is nonextractable by these solvents. The latter probably consists of aqueous-soluble (hydrophilic) metabolites as well as metabolites covalently bound to macromolecules. The metabolism of BP and the amount of covalently bound radioactivity increased with increasing periods of incubation of the cells with ^{3}H-BP. This finding and the fact that the metabolism of BP (1 μg/ml) was almost completely inhibited by 7,8-benzoflavone (3 μg/ml) at all time periods studied suggest that a time-dependent metabolism of BP is required for covalent binding to nuclear material. It is suggested that the binding of BP to subnuclear macromolecules may involve two steps. The marked localization of potent carcinogens such as BP and MNNG in fraction I suggests the existence of possible common nuclear sites for binding chemical carcinogens in general. (46 refs.)

77-4921 **Division of Fecal Stream and Colorectal Carcinogenesis.** (Eng) Winkler, R. (Chir. Univ.-Klinik, Abteilung fur Allgemeinchirurgie, Martinistrasse 52, D 2000 Hamburg 20, W. Germany); Heitmann, C.; Otto, H. F. *Chir Gastroenterol* 11(1): 105-108; 1977.

Gastrointestinal carcinogenesis by N-methyl-N-nitro-N-nitrosoguanidine (MNNG) was studied in male Wistar rats that had a double-loop colostomy of the descending colon. Rats with an intact or divided fecal passage were infused with 2 mg/kg MNNG 2x/wk for > 7 mo. The frequency of polyps and carcinomas was significantly reduced in the excluded colon (from 48 polyps or carcinomas in 29 rats with regular passage to 8 polyps in 29 animals with a colostomy), although the time of carcinogen contact was much longer in the excluded colon. All polyps were adenomatous, and most showed focal malignant lesions and infiltration. The cancers were mainly undifferentiated adenocarcinomas. All animals with a colostomy, even those not treated with MNNG, developed poorly differentiated adenocarcinomas at the oral stoma about 150 days postsurgery. To prove the effect of eversion on the colonic mucosa, the descending colon, which was excluded from fecal passage by an ascending colostomy, was divided and implanted in abdominal skin. Carcinomas developed equally both at the oral stoma of the colostomy and at the upper margin of the everted descending colon. This colostomy-cancer development may be caused by permanent mechanical irritation, loss of the protecting mucous layer, and/or licking of the stoma. (14 refs.)

77-4922 **Activation of Hepatic Guanylate Cyclase by N-Methyl-N′-nitro-N-nitrosoguanidine. Effects of Thiols, N-Ethylmaleimide, and Divalent Cations.** (Eng) DeRubertis, F. R. (Dept. Medicine, Veterans Admin. Hosp., Pittsburgh, PA 15240); Craven, P. A. *J Biol Chem* 252(16): 5804-5814; 1977.

The possibility that stimulation of the hepatic guanylate cyclase (GC)-guanosine 3′: 5′-monophosphate (cGMP) system by N-methyl-N′-nitro-N-nitrosoguanidine (MNNG) is linked to the thiol reactivity of this compound was investigated, and the actions of MNNG were compared to those of nitroprusside, an agent known to oxidize thiol groups. The actions of MNNG on soluble rat hepatic GC activity and on cellular cGMP were abolished or significantly suppressed by the thiol antioxidants dithiothreitol, glutathione, and cysteine and by ascorbate. Dithiothreitol, the most effective inhibitor, also completely reversed the increases in enzyme activity observed in hepatic supernatant fractions previously exposed to MNNG. The inhibitory effects of the thiols and ascorbate were optimally expressed by prior incubation of the antioxidants with MNNG, suggesting that direct interactions between MNNG and the antioxidants were involved in suppressing the GC response. The capacity of MNNG to activate the enzyme fell with continued incubation with antioxidant, indicating that activation of GC is mediated by labile decomposition products of MNNG. The -SH group alkylators, N-ethylmaleimide and maleimide, markedly suppressed MNNG and nitroprusside stimulation of GC and cGMP. These results indicate that stimulation of the hepatic GC-cGMP system by MNNG and nitroprusside involves interactions of these agonists or their derivatives with tissue-SH groups, and it could involve oxidation of these groups by reactive oxides of nitrogen, such as nitroxide radicals. (59 refs.)

77-4923 **Induction of Stomach Adenocarcinomas in Rats by the Combined Administration of the Precursors of N-Methyl-N-Nitroso-N′-Nitroguanidine.** (Rus) Kartasheva, L. A. (Dept. Tumor Modeling, Inst. Oncology Problems of Ukrainian SSR Acad. Sciences, Kiev, USSR). *Vopr Onkol* 23(8): 54-57; 1977.

Po administration of N-methyl-N′-nitroguanidine and sodium nitrite in the drinking water (1 mg/ml) to random-bred male mice for over 2 yr resulted in gastric adenocarcinomas in 43.7% of the rats surviving the 15.5 mo period until first tumor appearance. The gastric mucous membrane of rats without carcinomas showed morphological changes analogous to those induced by N-methyl-N-nitroso-N′-nitroguanidine (MNNG). It is suggested that MNNG is synthesized from precursors in the rat stomach. (17 refs.)

77-4924 **Use of Explant Culture to Study Pancreatic Carcinogenesis (Meeting Abstract).** (Eng) Resau, J. H. (Dept. Pathology, Univ. Maryland Sch. of Medicine, Baltimore, MD 21201); Jones, R. T.; Trump, B. F. *In Vitro* 13(3): 165; 1977. (no refs.)

77-4925 **Experimental Carcinoma of the Biliary Tract Induced in Dogs by N-Ethyl-N′-nitro-N-nitrosoguanidine.** (Eng) Nakazawa, S. (Second Dept. Internal Medicine, Nagoya Univ. Sch. Medicine, 65, Tsurumacho, Showa-ku, Nagoya, 466 Japan); Naito, Y.; Yamamoto, Y.; Yamase, H; Sobue, K.; Yamada, K.; Yamamoto, T.; Ichikawa, M.; Hidano, H.; Kachi, T.; Hayashi, S.; Kazikawa, M.; Hattori, T. *Gastroenterol Jpn* 12(2): 47-50; 1977.

Experimental biliary tract carcinoma was produced in eight mongrel dogs by infusing 5-10 mg of a 0.7- to 1.0-mg/ml solution of N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) through an external biliary fistula every day for a max of 180 days. The experiment was terminated prematurely in seven dogs (in 5 dogs the fistula was inadvertently pulled out and 2 dogs died of general weakness). Pathological changes were observed in the one surviving dog that had been given ENNG for 180 days and then sacrificed 192 days later. Macroscopically, scattered foci with a flat elevation were observed along the entire mucosal surface of the common bile duct, and there was a tiny polypoid projection at the terminal portion. Microscopically, this projection was identified as adenocarcinoma confined to the mucosa, with no local invasion across the bile wall and no distant metastasis. The areas of flat elevation showed marked mucosal hyperplasia and partial atypical papillary proliferation. Mucosal hyperplasia was also present in the intrahepatic bile ducts and the duodenum. It is concluded that ENNG is carcinogenic to the biliary system in dogs and that this experimental model would be useful for investigations of biliary tract carcinoma. (5 refs.)

77-4926 **Current NIOSH Intelligence Bulletin: 2-Nitropropane.** (Eng.) Finklea, J. F. (Natl. Inst. Occupational Safety and Health, Washington, DC) *Am Ind Hyg Assoc J* 38(7): A-15-A-19; 1977.

A recent inhalation study indicated that 2-nitropropane induces hepatocellular carcinoma or hepatic adenoma in rats. Various recommendations for limiting occupational exposure of humans, in whom the carcinogenic potential has not yet been proved, are presented. (5 refs.)

77-4927 **Sequential Morphologic Alterations in the Bronchial Epithelium of Syrian Golden Hamsters During N-Nitrosomorpholine-induced Pulmonary Tumorigenesis.** (Eng) Reznik-Schuller, H. (Abteilung fur Experimentelle Pathologie, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, 3 Hannover 61, W. Germany). *Am J Pathol* 89(1): 59-66; 1977.

The morphological alterations in the bronchial epithelium of male Syrian golden hamsters following weekly injections with 20% of the LD_{50} dose of N-nitrosomorpholine (NM) (98 mg/kg body wt) were examined by light and electron microscopy. As early as the 4th wk of the experiment, focal proliferations of the APUD (amine precursor uptake and decarboxylase) type cells were observed. With prolonged NM treatment, the cytoplasmic granules in these cells decreased in number and the cytoplasmic filaments increased. From wk 3 onward, Clara (non-ciliated) cells demonstrated intracytoplasmic formation of lamellar bodies. The number of these cells with lamellar bodies increased with treatment, and occasionally mature lamellar bodies were extruded into the bronchial lumen. Hyperplasia of nonciliated cells was noted in lobar and segmental bronchi after 15 wk. After 17 wk, pulmonary invasion by nonciliated cells was noted. One of two animals sacrificed after 20 wk of treatment had multiple pulmonary tumors. Thus NM causes the same alterations in APUD and Clara cells as N-diethylnitrosamine and N-dibutylnitrosamine; these changes are distinct from those induced by the hydrocarbons. (23 refs.)

77-4928 **Metabolism of Three Cyclic Nitrosamines in Sprague-Dawley Rats.** (Eng) Snyder, C. M. (Carcinogenesis Program, Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN); Farrelly, J. G.; Lijinsky, W. *Cancer Res* 37(10): 3530-3532; 1977.

The metabolism of nitrosopyrrolidine, nitrosohexamethyleneimine, and nitrosoheptamethyleneimine was studied in Sprague-Dawley rats. The three cyclic nitrosamines, which were administered by gavage, were labeled at the α carbon with ^{14}C. Radioactivity was measured in excreted CO_2 and urine. At low doses (2-4 mg/animal), the compounds were metabolized to $^{14}CO_2$ to the extent of 77%, 43%, and 27%, respectively, after 24 hr. At doses closer to the LD50 (70-160 mg/animal) the corresponding values were only 14%, 4%, and 8%, respectively, after 24 hr. These results suggest the existence of limited quantities of nitrosamine-metabolizing enzymes in the rat. (10 refs.)

77-4929 **Synthesis of the Selective Bladder Carcinogen, N-(*n*-Butyl)-N-(3-carboxypropyl)nitrosamine (BCPN).** (Eng.) Gaffield, W. (Western Regional Res. Center, Agricultural Res. Service, US Dept. Agriculture, Berkeley, CA 94710); Keefer, L. K.; Roller, P. P. *Org Prep Proced Int* (92): 49-52; 1977.

A short and efficient method for synthesizing the bladder carcinogen N-(n-butyl)-N-(3-carboxypropyl)-nitrosamine is described. (8 refs.)

77-4930 **Natural History of Intestinal Neoplasms Induced in Rats by a Single Injection of Methyl-(acetoxymethyl)nitrosamine.** (Eng.) Ward, J. M. (NCI, Bethesda, MD 20014); Rice, J. M.; Roller, P. P.; Wenk, M. L. *Cancer Res* 37(9): 3046-3052; 1977.

The natural history of intestinal tumors induced in 5-wk-old male Sprague-Dawley rats by a single ip injection (0.1 millimole/kg, 1/2 of the LD50) of methyl(acetoxymethyl)nitrosamine (DMN-OAc) is presented. From 70% to 90% of the rats developed tumors 20-50 wk after injection; 70%-86% had intestinal tumors, most commonly in the small intestine. Most of the latter were tubular adenocarcinomas that invaded the gut wall. The degree of invasion correlated with the size of the tumor. However, on reaching the serosa they usually became cystic and did not metastasize, even when they had grown very large. (21 refs.)

77-4931 **Accumulation of O^6-Methylguanine in Non-Target-Tissue Deoxyribonucleic Acid During Chronic Administration of Dimethylnitrosamine.** (Eng) Margison, G. P. (Paterson Labs., Christie Hosp., Withington, Manchester M20 9BX, England); Margison, J. M.; Montesano, R. *Biochem J* 165(3): 463-468; 1977.

The amounts of O^6-methylguanine (O^6-MG) in the DNA of target and nontarget tissues of BD rats were determined during chronic dimethylnitrosamine administration to discover to what extent repeated doses might result in the accumulation of O^6-MG. Male BD-IV rats were given ^{14}C-DMN (2 mg/kg) by stomach tube on 5 consecutive days/ wk. The rats were killed after 2, 4, 8, 16, and 24 wk of treatment (72 hr after final DMN dose), and DNA was isolated from the pooled livers, kidneys, and lungs. Purine bases were released from the DNA by mild acid hydrolysis and separated by Sephadex G-10 chromatography. Throughout the experiment, the content of 7-methylguanine in liver DNA was 16 times that in the kidney and lung. It increased in the DNA of all three tissues up to 16 wk, but by 24 wk it had decreased by 20% in the liver and 46% in the other tissues. O^6-MG was present in lung and kidney DNA after 4 wk of DMN administration, and it continued to increase throughout the experiment. No O^6-MG was detected in the DNA of liver even after 24 wk. The amount of O^6-MG in kidney and lung DNA increased relative to that of 7-MG, and by 24 wk was 60% of the 7-MG in both tissues. Incorporation of ^{14}C$_1$ breakdown products of DMN into normal purines in DNA increased continuously in all three tissues. The results indicate that chronic administration of DMN does not lead to a specific accumulation of O^6-MG in target organ DNA. They suggest that, although O^6-MG may be the critical product of alkylating carcinogens, the induction of tumors in certain tissues does not always correlate simply with its persistence or accumulation in DNA and that the effects of DNA synthesis or other alkylation products must be taken into account. (29 refs.)

77-4932 **Repressible and Inducible Enzymic Forms of Dimethylnitrosamine-Demethylase.** (Eng.) Arcos, J. C. (Seamen's Memorial Res. Lab., US Public Health Service Hosp., 210 State St., New Orleans, LA 70118); Davies, D. L.; Brown, C. E.; Argus, M. F. *Z Krebsforsch* 89(2): 181-199; 1977.

Two different forms of hepatic dimethynitrosamine demethylase (DMND) activity were investigated in Sprague-Dawley rats and Swiss-Webster, C3H/mai, A/He, AKR, BALB/c, C3H/He, C57B1/6, C57BL/10Sn, DBA/2, and SJL mice. Different enzyme responses at different DMN substrate concentrations were observed. Substrate concentrations up to 4 mM yielded the lowest line segment (enzyme I), those between 50 and 200 mM the highest line segment (enzyme II). The apparent Km values for the two line segments were 0.20 and 51 mM postmitochondrial fraction for the rat liver, and 0.28 and 44 mM for the mouse liver postmitochondrial fraction. Studies with isolated rat lung microsomes indicated that rat lung tissue contains $<$ 10% of the DMND activity of rat liver. A polychlorinated biphenyl Aroclor 1,254 (500 mg/hg ip) repressed enzyme I and induced enzyme II in rat liver. A less strong response was found in mice. Pretreatment with PB (4 consecutive daily doses of 80 mg/kg ip) brought about marked repression of enzyme I in both species, but it induced enzyme II only in the rat. Pretreatment with 3-methylcholanthrene (40 mg/kg ip) only repressed enzyme I in the rat. The differential response of DMND was paralleled by corresponding changes in Vmax. Beyond 300 mM, DMN decreased DMND activity, probably owing to protein denaturation. (57 refs.)

77-4933 **Activation of Intracisternal A Particles in Mouse Liver by Diethylnitrosamine.** (Eng.) Shinozuka, H. (Dept. Pathology, Univ. Pittsburgh Sch. Medicine, Pittsburgh, PA 15261) Estes, L. W. *J Natl Cancer Inst* 58(4): 1163-1166; 1977.

Livers of 6- to 7-wk-old male C3H/He, CBA, A, and BALB/c mice were examined by electron microscopy for the presence of intracisternal A particles (ICAP) after administration of diethylnitrosamine (DEN: 100 ppm) in drinking water. The ICAP were found in the livers of only two mice (strains C3H/He and A). By contrast, treatment of mice with DEN greatly enhanced the appearance of ICAP in the liver cells of all strains. Within 2 wk of treatment, ICAP were present in 8%-26% of liver cells in all mice, and the number of ICAP/cell ranged from 3 to 12. Aside from mild disorganization of the rough endoplasmic reticulum, such as segmentation and vesiculation, liver cells of carcinogen-treated mice showed none of the consistent abnormalities that characterize the appearance of ICAP. The reactivation of ICAP (which are usually suppressed in adult mice) by DEN may be a useful marker for analysis of the sequential alterations of the liver that lead to the development of hepatoma during carcinogenesis. (24 refs.)

77-4934 **In Vivo Carcinogen-induced Rat Liver Changes Studied In Vitro (Meeting Abstract).** (Eng)

Borenfreund, E. (Memoral Sloan-Kettering Cancer Center, New York, NY 10021). *In Vitro* 13(3): 181-182; 1977. (no refs.)

77-4935 **Activity of the Enzymes of Glycolysis and Gluconeogenesis in Primary Hepatomas Induced by Diethylnitrosamine.** (Rus) Kil'dema, L. A. (Inst. Experimental and Clinical Medicine, Ministry Public Health Estonian SSR, Tallinn, USSR); Teras, L. E.; Lond, M. E. *Vopr Med Khim* 23(4): 490-494; 1977.

The enzymes involved in glycolysis and gluconeogenesis were studied in C$_3$HA mice and rats with primary hepatomas induced by diethylnitrosamine. The tumors were mainly well differentiated hepatocellular adenomas. Hexokinase activity was increased about two-fold in the rat hepatomas and three-fold in the mouse hepatomas. Glucokinase was unaltered or slightly decreased and fructokinase activity was greatly decreased in primary hepatomas. The activities of glucose-6-phosphatase and fructose-1,6-diphosphatase were greatly decreased, especially the former. (20 refs.)

77-4936 **Altered Cobalamin Distribution in Rat Hepatomas and in the Livers of Rats Treated with Diethylnitrosamine.** (Eng.) Linnell, J. C. (Dept. Experimental Chemical Pathology, Vincent Square Labs. Westminster Hosp., London, SW1V, 2RH, England); Quadros, E. V.; Matthews, D. M.; Morris, H. P.; Poirier, L. A. *Cancer Res* 37(9): 2975-2978; 1977.

The distribution of cobalamin (Cbl) cofactors was investigated in transplanted Morris 7777 or 7800 hepatomas in Buffalo rats, and in the livers of Sprague-Dawley rats treated with the hepatocarcinogen diethylnitrosamine (DENA). DENA was administered chronically (100 ppm in drinking water for 3 wk) or acutely (25 mg ip). There was an increased proportion of methylcobalamine (Me-Cbl) in the livers and tumors of rats bearing the hepatomas compared to control rats. The total Cbl content of the hepatomas was significantly lower than that of host or control livers. Similarly, the total Cbl content of the livers from the tumor-bearers was less than that in controls. Acute DENA increased hepatic Me-Cbl only slightly. Liver wt was reduced, and the hepatic content of total Cbl fell to 55% of that in control rats. It is suggested that the folate cycle is involved in the regulation of Me-Cbl synthesis and, apart from acting as a cofactor in the methyltransferase system, Me-Cbl may directly or indirectly be involved in nucleic acid synthesis and cell proliferation. (41 refs.)

77-4937 **Rapid Emergence of Carcinogen-induced Hyperplastic Lesions in a New Model for the Sequential Analysis of Liver Carcinogenesis.** (Eng) Solt, D. B. (Dept. Pathology, Univ. Toronto, Toronto, Ontario, Canada M5S 1A8); Medline, A.; Farber, E. *Am J Pathol* 88(3): 595-610; 1977.

An in vivo assay system based on the phenomenon of selective resistance to cytotoxicity of carcinogen-altered cells has been developed. The system consists of three components: an initiator, diethylnitrosamine (DEN); a selective growth inhibitor, 2-acetylaminofluorene (2-AAF); and a generalized potent growth stimulus, in this case 67% partial hepatectomy (PH). After PH, the DEN-altered hepatocytes grew out as basophilic foci that were distributed randomly throughout the 2-AAF-suppressed parenchyma. Within 1 wk they could be seen as tiny, discrete, translucent nodules on the capsular and cut surface of the remaining lobes. By 6 wk, many basophilic foci had increased to 3 mm in diameter and were histologically similar to the hyperplastic liver nodules described in the literature. Hepatocellular carcinomas were found in animals sacrificed several months after completion of the experiment. Pulmonary metastases from these tumors were sometimes seen. On day 28, γ-glutamyltransferase activity was histochemically localized within the foci of proliferating hepatocytes. This system appears to result in relatively homogenous populations of altered cells. The ability to manipulate the interval between DEN-mediated initiation and 2-AAF-mediated selection, the duration of selection, and the conditions that exist during both processes may help clarify several aspects of liver carcinogenesis. (52 refs.)

77-4938 **Binding of 9-^{14}C-2-Acetylaminofluorene with Rat Liver Nucleic Acids During Hepatocarcinogenesis and in Primary Hepatomas.** (Rus) Ivanov, S. D. (Lab. Biochemistry, N. N. Petrov Scientific Res. Inst. Oncology of the USSR Ministry of Public Health, Leningrad, USSR); Dzhioev, F. K. *Biull Eksp Biol Med* 83(3): 332-334; 1977.

Residual binding of ^{14}C-2-acetylaminofluorene (^{14}C-AAF) to male albino random-bred rat liver nucleic acids was investigated following tumor induction by AAF or diethylnitrosourea administered in the diet. Ip injection of 0.13 μCi/kg ^{14}C-AAF resulted in increased binding of AAF to tumorous liver, as compared to normal liver, up to 6 mo after initiation of carcinogenesis. The binding of ^{14}C-AAF to the DNA in primary hepatomas was mainly due to the RNA heterodispersed components in the 18S fraction, as well as to the polyadenylate-enriched 10S and 5S fractions. (10 refs.)

77-4939 **Strand Breaks in DNA from Normal and Transformed Human Cells Treated with 1,3-Bis(2-chloroethyl)-1-nitrosourea.** (Eng) Erickson, L. C. (Lab. Molecular Pharmacology, Div. Cancer Treatment, NCI, NIH, Bethesda, MD 20014); Bradley, M. O.; Kohn, K. W. *Cancer Res* 37(10): 3744-3750; 1977.

The DNA of human cells treated with 1,3-bis(2-choloroethyl)-1-nitrosourea (BCNU) was examined for the appearance of single-strand breaks or alkali-labile sites. Normal human embryo fibroblasts (WI-38) were compared with simian virus 40-transformed derivative line (VA-13), which had an increased sensitivity to the cytotoxic actions of the drug. BCNU induced single-strand breaks and/or alkali-labile sites in both cell types, as measured by alkaline sedimentation at pH 13 or by alkaline elution at pH 12.1. However, break frequencies (which may include alkalilabile sites) were greater when measured by alkaline sedimentation than when measured by alkaline elution. Alkaline sedimentation disclosed more breaks in WI-38 than in VA-13 cells, but alkaline elution indicated the opposite. The results may reflect differences between the two cell types in the relative frequencies of drug-induced alkali-labile sites as opposed to actual single-strand breaks. The DNA breaks and/or alkali-labile sites appeared to be repaired when drug treatment medium was replaced with fresh medium. If the medium was not replaced, there was no repair, even after times much longer than the reported half-times for BCNU decomposition. This might be due to an inhibitory effect of a relatively stable drug product or to a stimulatory effect of fresh medium. The apparent rates of repair were similar in the two cell types studied. (22 refs.)

77-4940 **Tumors in Two Generations of Mice in Different Environmental Conditions.** (Eng) Mookenthottathil, T. (Inst. Cancer Res., Univ. Vienna, Borschkegasse 8a, 1090 Vienna IX, Austria). *Oncology* 34(5): 201-204; 1977.

The influence of environmental carcinogens on the developing embryo was investigated using Swiss albino mice as models and 1-ethyl-1-nitrosourea (ENU) as the carcinogen. The percentage of tumors developing among the F1 siblings delivered and nursed by mothers treated with ENU (60 mg/kg, ip) was higher than that of the F1 siblings delivered of treated mothers but nursed by untreated foster mothers. The presence of multiple tumors was also more frequent in the first group compared with the second. The second generations also developed malignant tumors. In two successive generations of siblings delivered of untreated mothers but nursed by foster mothers treated with ENU on the 12th day of pregnancy, the tumor percentage was higher than in the control group. This result is significant since the siblings were not exposed to the carcinogen transplacentally, and the foster mothers were treated with only a single dose of ENU long before the lactating period. (28 refs.)

77-4941 **Use of the Beta-Binomial Distribution in Dominant-lethal Testing for "Weak Mutagenic Activity". Part 1.** (Eng.) Aeschbacher, H. U. (Nestle Products Technical Assistance Co., Ltd., Biological Lab., CH-1350 Orbe, Switzerland) Vuataz, L.; Sotek, J.; Stalder, R. *Mutat Res* 44(3): 369-390; 1977.

In a dominant-lethal test for weak mutagenic activity in Swiss mice given a methylurea-sodium nitrite solution, a beta-binomial distribution provided a better fit than a binomial distribution for data bases on a large number of counts of dead and total implants. The problem of whether male or female animals should be considered as the experimental units is discussed, and calculations are presented. (31 refs.)

77-4942 **Effects of Altered Thyroid States on Mammary Tumor Growth and Pituitary Gland Function in Rats.** (Eng) Cave, W. T. (Dept. Internal Medicine, Div. Endocrinology, Univ. Virginia Sch. Medicine, Charlottesville, VA 22901); Dunn, J. T.; MacLeod, R. M. *J Natl Cancer Inst* 59(3): 993-999; 1977.

The effects of altered thyroid states on mammary tumor growth and pituitary gland function were studied in 50-day-old inbred BUF/N rats given N-nitrosomethylurea (NMU, 50 mg/kg iv during weeks 1, 5, and 9). When the animals were killed 3 mo after the initial dose of NMU, no differences in tumor incidence or in DNA synthesis by in vitro tumor slices were seen among the controls (euthyroid treatment group), rats given propylthiouracil [PTU, 8 mg/deciliter (dl) in their drinking water, hypothyroid group], or rats given thyroxine (T4, 125 μg/dl in drinking water, hyperthyroid group). In further experiments, mammary tumors were transplanted sc into the inguinal region of 1-wk-old euthyroid, hypothyroid, and hyperthyroid rats. Hypothyroid and euthyroid animals showed the same level of tumor growth, but hyperthyroid animals experienced an increase. These results suggest that hypothyroidism-induced alterations in pituitary thyrotropin, growth hormone, and prolactin metabolism do not enhance the growth of mammary tumors. (50 refs.)

77-4943 **Epithelial-Stromal Interaction in Relation to Normal and Abnormal Differentiation of the Urothelium In Vitro (Meeting Abstract).** (Eng) Hodges, G. M. (Imperial Cancer Research Fund, London WC2, England). *In Vitro* 13(3): 178; 1977. (no refs.)

77-4944 **Acid Hydrolase and Cytochrome Oxidase Activities in Nitrosourea Induced Tumors of the Nervous System.** (Eng) Allen, N. (Div. Neurology, Coll. Medicine, Ohio State Univ., Columbus, OH 43210); Clendenon, N. R.; Abe, H.; Swenberg, J. A.; Koestner, A.; Wechsler, W.; Shuttleworth, E. C. *Acta Neuropathol (Berl)* 39(1): 13-23; 1977.

Acid hydrolase and cytochrome oxidase activities were studied in samples from 57 nitrosourea-induced neuroectodermal tumors in rats (7 ependymomas, 13 anaplastic or mixed gliomas, 7 gliosarcomas, 1 meningioma, 20 well-differentiated or anaplastic schwannomas, and 9 nervous system sarcomas). The activities of β-glucuronidase, acid phosphatase and glucosaminidase were high in all tumors; arylsulfatase differed in that it was markedly elevated among the gliomas but not in the nonglial tumors. Hydrolase activities were present in all tumor zones, including those of regression, viable solid growth, and proliferation and invasion. Acid hydrolase activities were predominantly particulate and probably lysosomal in localization. Cytochrome oxidase activities were markedly decreased in all tumors. Although phagocytosis or regression undoubtedly contributes to the total enzyme activity of the tumor, it is not the sole source. The hydrolase activities appear early in tumor development and persist through late growth. The function of these enzymes may relate to accelerated growth and cell turnover, to degradation of organelles, and to pinocytotic ingestion of macromolecules. (50 refs.)

77-4945 **Induction of Tumors of Peripheral Nervous System in Female Donryu Rats by Continuous Oral Administration of 1-Methyl-1-nitrosourea.** (Eng) Ogiu, T. (Dept. Chemical Pathology, Natl. Inst. Hygienic Sciences, Kamiyoga 1-18-1, Setagaya-ku, Tokyo 158, Japan); Nakadate, M.; Furuta, K.; Maekawa, A.; Odashima, S. *Gann* 68(4): 491-498; 1977.

The ability of 1-methyl-1-nitrosourea (MNU) to induce peripheral nervous system (PNS) tumors was investigated in female Donryo rats given 400, 200 or 100 ppm MNU in the drinking water (groups 1, 2, and 3, respectively). The MNU was administered every day for 4 wk and 5 days/wk after the 5th wk until the rats died or were killed for autopsy. The last rat was killed on day 208. In group 1, 18/27 rats developed tumors: 12 in the nervous system (5 CNS, 11 PNS), 12 in the digestive tract, 2 in hematopoietic organs and 1 in the kidney. In group 2, 30/33 animals developed tumors: 30 in the nervous system (10 CNS, 27 PSN), 1 in the digestive tract, and 1 each in the sc tissue, heart and vagina. In group 3, 35/36 animals developed tumors: 33 in the nervous system (14 CNS, 31 PNS), 2 in the digestive tract, 4 in hematopoietic organs, 4 in the mammary glands and 1 each in the kidney, sc tissue, heart, uterus, spleen, thyroid, and mediastinum. In general, tumors of the spinal nerve roots were most frequent. The av survival was 143.6, 162.3 and 170.0 days for groups 1, 2, and 3, respectively. The histology of the various tumors is presented. (24 refs.)

77-4946 **Suppression of NMU-Induced Mammary Cancer by Vitamin A Acetate (Meeting Abstract).** (Eng.) Grubbs, C. J. (IIT Res. Inst., Chicago, IL 60616) Moon, R. C.; Sporn, M. B.; Goodman, D. G. *Proc Am Assoc Cancer Res* 18: 171; 1977. (no refs.)

77-4947 **Influence of Dietary Fat on the Induction of Mammary Tumors by N-Nitrosomethylurea: Associated Hormone Changes and Differences Between Sprague-Dawley and F344 Rats.** (Eng) Chan, P. C. (Naylor Dana Inst. for Disease Prevention, American Health Foundation, Valhalla, NY 10595); Head, J. F.; Cohen, L. A.; Wynder, E. L. *J Natl Cancer Inst* 59(4): 1279-1283; 1977.

The effect of various concentrations of N-nitrosomethylurea (NMU) on female Sprague-Dawley and F344 rats, the influence of dietary fat on tumor incidence, and tumor-associated changes in serum hormone levels were investigated. Rats from each strain were inoculated iv with either 50 mg/kg at 50 days of age or with two doses, at days 50 and 80 of either 25 mg/kg or 12.5 mg/kg each. Rats from each group were then fed either a high fat (HF: 20% lard, 44% sucrose) or a low fat (LF: 5% lard, 59% sucrose) diet. The experiment was terminated 6 mo after the first dose of NMU. The mammary tumor incidence in Sprague-Dawley rats fed 50, 25, and 12.5 mg MNU, respectively, was as follows: HF - 184 + 5 kidney tumors, LF - 134 + 1 leukemia and 8 kidney tumors; HF - 121 + 1 leukemia and 2 kidney tumors, LF - 92 + 3 leukemia and 2 kidney tumors; HF - 0 and LF- 0. The incidence of mammary tumor for F344 rats at the same respective doses was as follows: HF - 49 + 1 leukemia and 2 kidney tumors, LF - 10 + 4 kidney tumors; HF - 14, LF - 12; HF- 0, LF - 0. Thus Sprague-Dawley rats were more sensitive to MNU, but rats fed a HF diet were more susceptible than those fed a LF diet regardless of strain. This enhancing effect was unrelated to body wt. Hormone levels were determined in F344 rats. At metestrus-diestrus, both the prolactin and estrogen levels were significantly higher in animals fed the HF diet than the LF diet. A comparison of prolactin estrogen ratios indicated that animals with tumors had higher ratios than those without tumors, regardless of diet or estrous cycle. There was no correlation between prolactin and estrogen levels in individual animals, regardless of diet or estrous cycle. (17 refs.)

77-4948 **Hormonal Influence on Growth and cAMP Levels in a Rat Mammary Adenocarcinoma Cell Line (Meeting Abstract).** (Eng) Chan, P. C. (American Health Foundation, Valhalla, NY 10595); Head, J.; Tsuang, J. *In Vitro* 13(3): 190; 1977. (no refs.)

77-4949 **The Importance of Synergy Between Weak Carcinogens in the Induction of Bladder Cancer in Experimental Animals and Humans.** (Eng) Hicks, R. M.

(Sch. Pathology, Middlesex Hosp. Medical Sch., London, W1P 7LD, England); Chowaniec, J. *Cancer Res* 37(8, part 2): 2943-2949; 1977.

The synergism between sodium cyclamate or sodium saccharin and N-methyl-N-nitrosourea (MNU) in the induction of bladder carcinogenesis was investigated in Wistar rats. There were four groups of rats: (1) controls; (2) those receiving either saccharin (2.0 or 4.0 g/kg/day) or cyclamate (1.0 or 2.0 g/kg/day) in drinking water; (3) rats receiving 1.5 mg MNU instilled into the bladder and then either left untreated or fed saccharin or cyclamate in the diet at the same doses as Group 2; and (4) rats given 2-naphthylamine by stomach tube at a dose rate of 300 mg/kg/wk for 1 yr. Three tumors were induced in the rats fed 4.0 g saccharin; one tumor was induced in rats fed 1.0 g cyclamate, two in rats fed 2.0 g cyclamate. No tumors were found in controls, rats fed 2.0 g saccharin, or rats receiving MNU only. There was a 52% incidence of tumors in rats receiving MNU plus saccharin and a 50% incidence in rats receiving MNU plus cyclamate. Five of 17 rats in the 2-naphthylamine-treated group had bladder tumors. These results are from too small an experimental group to be statistically significant, but they do suggest that saccharin and cyclamate are powerful promotors of tumor growth. The extrapolation of these results to humans is discussed. (43 refs.)

77-4950 **Artificial Sweeteners and Human Bladder Cancer.** (Eng.) Howe, G. R. (Epidemiology Unit, Natl. Cancer Inst. Canada, Univ. Toronto, Ontario, Canada); Burch, J. D.; Miller, A. B.; Morrison, B.; Gordon, P.; Weldon, L.; Chambers, L. W.; Fodor, G.; Winsor, G. M. *Lancet* 2(8038): 578-581; 1977.

A study on the correlation between the use of artificial sweeteners and bladder cancer was conducted based on the results of questionnaires obtained from 480 men and 152 women with bladder cancer. The risk ratio for men who had used the sweeteners vs those who had never used them was 1.6; there was a significant dose-response relationship for both the duration and frequency of use. Joint controlling for both smoking and instant coffee consumption were used so that the relationship between these variables and artificial sweetener consumption was independent. It was not possible to determine the composition of each artificial sweetener used since the composition of saccharin and/or cyclamate had changed over the years; however, 82% of the men reported the use of saccharin only. Male diabetics who did not use sweeteners were at a decreased risk, but those who did use them had the same risk as the nondiabetic men. For women, there was a nonsignificant decreased use of artificial sweeteners among the cancer cases. (15 refs.)

77-4951 **Potentiation of the Action of Azaserine on the Rat Pancreas by Raw Soya Bean Flour.** (Eng.) Morgan, R. G. (Univ. Dept. Therapeutics, Ninewells Hosp., Dundee DD2 1UB, Scotland) Levinson, D. A.; Hopwood, D.; Saunders, J. H.; Wormsley, K. G. *Cancer Lett* 3(1/2): 87-90; 1977.

Male Wistar rats were fed raw soya flour to induce pancreatic hypertrophy, and they also received weekly ip injections of azaserine (5 mg/kg), a pancreatic carcinogen. The combined treatment resulted in the development of large numbers of hyperplastic nodules in the acinar tissue of the rat pancreas. It is concluded that the rat pancreas stimulated to proliferate by raw soya flour provides a sensitive model for detecting and studying pancreatic carcinogens. (6 refs.)

77-4952 **A Protective Effect of Caffeine on Drosophila Larvae Treated with Methyl Methanesulfonate.** (Eng) Nigsch, J. (Dept. Zoology, Swiss Federal Inst. Technology, Zurich, Switzerland); Wurgler, F. E.; Graf, U. *Mutat Res* 45(1): 41-45; 1977.

The effects of treatment of *Drosophila melanogaster* with caffeine, methyl methanesulfonate, and with a mixture of the two were investigated. The mixture of the two was less toxic than expected from the observed treatment with either substance alone. Caffeine may inhibit DNA replication, allowing more time for DNA repair by a caffeine insensitive repair mechanism. (14 refs.)

77-4953 **Mutagenicity Studies on Chemical Carcinogens (Meeting Abstract).** (Eng) Clive, D. (Burroughs Welcome Co., Research Triangle Park, NC 27709). *In Vitro* 13(3): 191; 1977. (no refs.)

77-4954 **Effect of Coffee on Carcinogenicity of Cycasin.** (Eng.) Mori, H. (Dept. Pathology, Gifu Univ. Sch. Medicine, 40 Tsukasamachi, Gifu 500, Japan); Hirono, I. *Br J Cancer* 35(3): 369-371; 1977.

Sprague-Dawley rats received a coffee solution instead of drinking water and/or a single dose of cycasin (150 mg/kg po). Rats that received both coffee and cycasin showed a high incidence of tumors, particularly colorectal adenomas. Tumors were scarce in rats given coffee or cycasin alone. (11 refs.)

77-4955 **Enhancement of Mutagenesis In Vitro by a Tumor Promoting Agent (Meeting Abstract).** (Eng) Lankas, G. R. (Kettering Lab., Univ. Cincinnati, Cincinnati, OH 45267); Christian R. T.; Baxter, C. S. *In Vitro* 13(3): 193; 1977. (no refs.)

77-4956 **Tumor Promoters Inhibit Spontaneous and Induced Differentiation of Murine Erythroleukemia Cells in Culture.** (Eng.) Yamasaki, H. (Coll. Physicians and Surgeons, Columbia Univ., New York, NY 10032); Fibach, E.; Nudel, U.; Weinstein, I. B.; Rifkind, R. A.; Marks, P. A. *Proc Natl Acad Sci USA* 74(8): 3451-3455; 1977.

12-O-Tetradecanoyl-phorbol-13-acetate (TPA) and certain congeners were found to be potent reversible inhibitors of both the spontaneous differentiation and differentiation induced by hexomethylene bisacetamide (HMBA), dimethyl sulfoxide, and butyric acid in murine erythroleukemia cells (MELC). The inhibition was unrelated to cytotoxicity. Derivatives of these compounds that are inactive in tumor promotion did not inhibit MELC differentiation. TPA inhibited HMBA-induced differentiation only if added at or just prior to the time of commitment (ability of an inducible strain of MELC to continue to differentiate after removal of the inducer). Delaying the addition of TPA decreases the inhibitory effect at a rate that is inversely related to the rate of appearance of committed cells. The mechanism by which TPA inhibits differentiation is not known. Inhibition of differentiation of MELC by TPA is associated with a decrease of globin messenger RNA (mRNA). (38 refs.)

77-4957 **Dissociation of Tumor Promoter-stimulated Ornithine Decarboxylase Activity and DNA Synthesis in Mouse Epidermis In Vivo and In Vitro by Fluocinolone Acetonide, a Tumor-promotion Inhibitor.** (Eng) Lichti, U. (In Vitro Pathogenesis Section, Experimental Pathology Branch, Div. Cancer Cause and Prevention, NCI, Bethesda, MD 20014); Slaga, T. J.; Ben, T.; Patterson, E.; Hennings, H. Yuspa, S. H. *Proc Natl Acad Sci USA* 74(9): 3908-3912; 1977.

The association between the tumor promotor 12-O-tetradecanoyl phorbol-13-acetate (TPA), orinithine decarboxylase (ODC) activity and fluocinolone acetonide (FA) inhibition of tumor promotion was investigated in female Charles River CD-1 mice and epidermal cultures from BALB/c mice. FA inhibited TPA-induced stimulation of DNA synthesis in vitro when added either before the TPA or after the exposure. The degree of inhibition increased with duration of FA pretreatment, but the presence of FA in the medium was not necessary to inhibit promotor action. In studies investigating the effect of FA on ODC responsiveness, 10 μg of FA was applied to mouse skin 5 min before 10 μg of TPA, and a potentiation of ODC response was observed. FA itself did not induce and had no effect on unstimulated ODC activity. This potentiation could also be demonstrated in vitro. The FA inhibition of TPA-induced DNA synthesis in vitro could be negated by treatment with exogenous putrescine. It is suggested that FA reduces cellular sensitivity to polyamines or causes their loss. (38 refs.)

77-4958 **The Effect of Phorbol Diesters on Chicken Embryo Fibroblasts.** (Eng) Driedger, P. E. (Dept. Pharmacology, Harvard Medical Sch., Boston, MA 02115); Blumberg, P. M. *Cancer Res* 37(9): 3257-3265; 1977.

Changes in chick embryo fibroblasts (CEF) that accompany or precede the decrease in large, external transformation-sensitive protein following treatment with the tumor promotor phorbol myristate acetate (PMA) are reported. With 30 nanograms (ng)/ml PMA, the CEF cells assumed a thinner, more elongated shape than controls, and they were scattered randomly across the plate or on top of one another. These changes were accompanied by a decrease in volume. The protein content per normal CEF with or without PMA treatment paralleled the volume results. Thus, the volume decrease was not due to the loss of water, but was associated with a change in cellular composition. The effects on morphology, volume, and the protein content were reversible. The exponential growth of CEF cultures in 50 ng/ml PMA was not significantly altered, but the cells did reach a 1.8-fold higher density than controls. Mitogenic stimulation with PMA was dose-dependent. Treatment of resting CEF with 30 ng/ml PMA caused a marked increase in 2-deoxy-D-glucose uptake relative to controls. This increase showed a classic dose-response relationship. The use of other phorbol derivatives to stimulate 2-deoxy-D-glucose uptake resulted in similar max effects, with the linear portions of the dose-response curves being basically parallel. However, phorbol itself was not active. These findings indicate that nanomolar concentrations of PMA can elicit responses in CEF similar to those caused by Rous sarcoma virus transformation. (47 refs.)

77-4959 **Focal Nodular Hyperplasia of the Liver Associated with High-Dosage Estrogens.** (Eng.) Aldinger, K. (Div. Gastroenterology, Univ. Texas Medical Sch. at Houston, P O Box 20708, Houston, TX 77025); Ben-Menachem, Y.; Whalen, G. *Arch Intern Med* 137(3): 357-359; 1977.

A 32-yr-old woman developed benign hyperplasia of the liver after receiving high-dose estrogen therapy for 3 yr. Following resection of the left liver lobe, she was continued on estrogen for 14 mo until a second angiogram revealed the development of a new lesion. Four mo after estrogen was stopped, the large liver nodule disappeared and smaller ones decreased. (23 refs.)

77-4960 **The Role of Tissue Interactions in Normal and Abnormal Urogenital Development in Mice (Meeting Abstract).** (Eng) Cunha, G. R. (Univ. Colorado, Denver, CO 80262). *In Vitro* 13(3): 178-179; 1977. (no refs.)

77-4961 **Chromosomal Changes in Rat Pituitary and Bone Marrow Induced by Long-Term Estrogen Administration.** (Eng) Malkova, J. (3rd Medical Dept. Charles Univ., Lab Endocrinology and Metabolism, Charles Univ., 128 08 Prague, Czechoslovakia); Michalova, K.; Pribyl, T.; Schreiber, V. *Neoplasma* 24(3): 277-284; 1977.

Chromosomal changes in the initial stage of estrogen-induced pituitary tumor formation, ie, during transition of the hyperplastic reaction of the gland into an autonomous tumor, were evaluated. Pituitary wt, mitotic index, and karyotypes of pituitary and bone marrow cells were studied in male Wistar rats after repeated injections of 1 mg estradiol benzoate. The animals were sacrificed at various times ranging from 7 to 210 days. In response to treatment, all rats had anemia and a marked decrease in body wt, but the pituitary wt started to rise, even during the first week. It increased gradually up to day 60, when there was a new considerable increase (tumor formation) in some animals. The large pituitary tumors (100-300 mg vs 6-8 mg for the resting gland) that resulted were highly vascularized. The mitotic index increased until day 90, when it diminished; most of the dividing cells were replaced by chromatin clusters with partial or total destruction of chromosomes. Most of the hyperplastic pituitary cells maintained a normal diploid karyotype, but a limited number of abnormal stem lines with marker chromosomes appeared during the early stages of pituitary hyperplasia. In later stages, the tumors were characterized by an increased number of aneuploid cells. Hormone treatment lowered the mitotic index of the bone marrow cells without any detectable change in karyotype. (20 refs.)

77-4962 **Mammary Tumorigenesis in Female C3H Mice** Fed Diets Containing Diethylstilbestrol or 17β-Estradiol (Meeting Abstract). (Eng.) Norvell, M. J. (Molecular Biology Div., Natl. Center for Toxicological Res., Jefferson, AR); Shellenberger, T. E. *Toxicol Appl Pharmacol* 41(1): 179; 1977. (no refs.)

77-4963 **Effects of Perinatal Estrogen on Mouse Mammary Response to Corticoids In Vitro.** (Eng) Warner, M. R. (Dept. Cell Biology, Baylor Coll. Medicine, Houston, TX 77030); Warner, R. L. *In Vitro* 13(8): 477-483; 1977.

The effects of adrenal corticoids on in vitro mammary differentiation were compared in neonatally estrogenized (E) and uninoculated control (N) BALB/c Crgl female mice. Newborn E mice were given 17β-estradiol (10 μg/day sc, x 5). At 4 wk of age, all mice were pretreated with 17β-estradiol (1 μg/day sc, x 9) and progesterone (1 mg/day sc, x 9). Groups of 10 or more entire mammary glands were then organ-cultured for 5 days with various combinations of mammotropin (M), somatotropin (S), insulin (I), and thyroxine (T) and with one of three adrenal corticoids: corticosterone (B), aldosterone (A), or cortisol (F). With each of the corticoids tested, E tissues formed more alveoli and more lobules in vitro than did N tissues. Differential development for both E and N tissues followed a quantitative pattern of MSIT < BMSIT < AMSIT < FMSIT. These findings suggest that the effects of exogenous corticoid-containing compounds on the effects of endogenous hormone release following stress may be amplified in individuals exposed to estradiol early in life. (12 refs.)

77-4964 **Epoxidation of the Stilbene Double Bond, a Major Pathway in Aminostilbene Metabolism.** (Eng.) Metzler, M. (Institut fur Pharmakologie und Toxicologie, Universitat Wurzburg, D-8700 Wurzburg, W. Germany) Neumann, H. G. *Xenobiotica* 7(3): 117-132; 1977.

The isolation and structural characterization of some new products in the metabolism of the carcinogen aminostilbene are described. A new and qualitatively different pathway in stilbene amine metabolism was found that may also have application for other stilbene derivatives. (36 refs.)

77-4965 **Effects of Diet on Conversion of Aflatoxin B_1 to Bacterial Mutagen(s) by Rats In Vivo and by Rat Hepatic Microsomes In Vitro.** (Eng) Suit, J. L. (Center Cancer Res., Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA 02139); Rogers, A. E.; Jetten, M. E.; Luria, S. E. *Mutat Res* 46(5): 313-323; 1977.

A lipotrope-deficient, high-fat diet, which enhances aflatoxin B_1 (AFB_1) hepatocarcinogenesis in rats, influenced the conversion of AFB_1 to mutagens detectable in the Ames Salmonella mutagenesis test system in two ways. First, in the urine of Sprague-Dawley and Fischer rats fed the lipotrope-deficient diet and given a single dose of AFB_1 (3 mg/kg), the proportion of mutagenic material that did not require activation by hepatic microsomes was higher than that in the urine of rats fed an adequate diet. Second, hepatic microsomal preparations (S-9 fractions) from deficient animals showed significantly lower activity in the in vitro conversion of AFB_1 to mutagen(s) than did S-9 fractions from normal animals. The S-9 fractions from deficient animals actually suppressed the activity of normal S-9 fractions in a mixed mutagenesis assay. The inconsistency of the second finding with the enhanced sensitivity of deficient animals to AFB_1 carcinogenesis suggests the need for caution in using in vitro mutagenesis tests for quantitative estimation of carcinogenic potency. (23 refs.)

77-4966 **Maintenance of Cytochrome P-450 and Metabolism of Aflatoxin B_1 in Primary Hepatocyte**

Cultures. (Eng) Decad, G. M. (Dept. Environmental Toxicology, Univ. California, Davis, CA 95616); Hsieh, D. P.; Byard, J. L. *Biochem Biophys Res Commun* 78(1): 279-287; 1977.

Primary hepatocyte cultures isolated from male Sprague-Dawley rats were maintained in a defined medium containing several hormones that would enable the cells to maintain an in vivo level of cytochrome P-450. Aflatoxin B_1 (AFB_1) was then added to the cultures and its metabolism was studied to determine whether the data obtained could be extrapolated to the in vivo state. These hepatocyte cultures completely metabolized AFB_1 in 10 hr, producing mostly water-soluble metabolites. In agreement with in vivo results, AFB_1 was the only nonpolar metabolite found. A significant portion of AFB_1 was covalently bound to cell constituents, which may be the basis for its toxicity and carcinogenicity. It is concluded that primary hepatocytes, in a defined culture medium supplemented with hormones, are a good model of the liver in studying the metabolism and toxicology of environmental carcinogens such as AFB_1. (18 refs.)

77-4967 **Effect of Aflatoxin B_1 and Corticosterone on Ribosome-Distributions Between Free and Membrane-bound States and Between Monosomes and Polysomes in Mouse Liver.** (Eng) Umemura, Y. (Natl. Inst. Animal Health, Kodaira-shi, Tokyo, Japan); Inoue, T.; Takagi, M. *Agric Biol Chem* 41(7): 1269-1273; 1977.

Changes of ribosome distributions in liver cells of mice treated with aflatoxin B_1 (AFB_1) alone or together with corticosterone were determined by discontinuous sucrose density gradient centrifugation. Male C3H/He mice were inoculated with AFB_1 (15 mg/kg) or with AFB_1 and corticosterone (15 mg/kg) and sacrificed 7 days later. The postmitochondrial fractions were obtained and analyzed. Membrane-bound ribosomes were decreased and free ribosomes increased in the livers of AFB_1-treated rats. Injection of corticosterone plus AFB_1 prevented this change in ribosome distribution between the free and membrane-bound states. The marked increase in monosomes and decrease in polysomes that occurred in the livers of AFB_1-treated mice were also prevented by simultaneous injection of corticosterone. Injection of actinomycin D produced the same results as AFB_1. It is concluded that AFB_1 causes structural changes in the microsomal membrane that lead to the release of polysomes from the membrane, resulting in degradation of the polysomes into monosomes. Ribosome-membrane interaction may have an important regulatory function in protein biosynthesis. (14 refs.)

77-4968 **Late Polysome Disaggregation by Aflatoxin B1 (Meeting Abstract).** (Eng.) Hayes, L. C. (Univ. Kansas, Lawrence, KS 66044). *Diss Abstr Int [B]* 38(2): 601; 1977. (no refs.)

77-4969 **Effect of Patulin on Krebs Cycle Intermediate-stimulated Oxygen Consumption (Meeting Abstract).** (Eng.) Hayes, A. W. (Dept. Pharmacology and Toxicology, Univ. Mississippi Medical Center, Jackson, MS). *Toxicol Appl Pharmacol* 41(1): 165; 1977. (no refs.)

77-4970 **Mutagenic Activity of Hymenovin, a Sesquiterpene Lactone from Western Bitterweed.** (Eng.) MacGregor, J. T. (U.S. Dept. Agriculture, Agriculture Res. Service, Western Regional Res. Lab., Berkeley, CA 94710) *Food Cosmet Toxicol* 15(3): 225-227; 1977.

Hymenovin, the major toxin of *Hymenoxys odorata*, was mutagenic in *Salmonella typhimurium* strains TA100 and TA98. The mutagenicity was not altered significantly by an in vitro rat liver metabolizing system. Tenulin and helenalin, two other sesquiterpene lactones, were not mutagenic in these *Salmonella* tester strains. (13 refs.)

77-4971 **Cannabinoids and Chromosomes (Meeting Abstract).** (Eng) Matsuyama, S. S. (Veterans Administration Hospital (Brentwood), Los Angeles, CA 90073); Fu, T. K.; Jarvik, L. F. *In Vitro* 13(3): 165; 1977. (no refs.)

77-4972 **Cigarette Smoke: Inducer of Glucuronide Synthesis in the Isolated Perfused Rat Lung.** (Eng) Uotila, P. (Dept. Physiology, Univ. Turku, SF-20520 Turku 52, Finland); Hartiala, J.; Aitio, A. *Toxicol Appl Pharmacol* 41(2): 445-448; 1977.

The effect of cigarette smoke on glucuronide synthesis in the isolated perfused rat lung was investigated. Adult male Wistar rats were exposed to the smoke of one filter cigarette daily for 10 consecutive days. On the 11th day, the lungs were perfused for 3 hr with a medium containing 4-methylumbelliferone. During perfusion, samples were taken from the perfusate and the amount of 4-methyllumbelliferylglucuronide was determined. The glucuronide formation rate was 90 nanomoles (nmol)/hr/lung for smoke-exposed rats and 55 nmol/hr/lung for control rats. Pulmonary microsomal uridine diphosphate glucuronosyltransferase activities were 200 and 150 nmol/hr/lung in smoke-exposed and control rats, respectively. The glucuronide conjugation rates in the perfusions were about half of those expected from microsomal enzyme assays. (18 refs.)

77-4973 **Development of Tumours in Syrian Hamster During Prolonged Experimental Exposure to**

Nas. (Eng) Kiseleva, N. S. (Dept. Epidemiology and Malignant Tumours, Inst. Experimental and Clinical Oncology, Acad. Medical Sciences of USSR, Karsirskoe sosse 6, Moscow, USSR); Milievskaja, I. L.; Caklin, A. V. *Bull WHO* 54(6): 597-605; 1977.

The carcinogenicity of nas was investigated in Syrian hamsters. The composition of the nas was: tobacco 45%, lime 8%, ash 30%, plant oil 12%, and water 5%. There were four experimental groups. In Group I, nas was administered as a dry powder to the left buccal pouch. In Group IIa and IIb, nas was administered as a suspension in sunflower oil; in group IIb, the administration was continued for six generations. In Group III, a nas suspension was introduced into the esophagus by a pneumothorax needle. In Group IV, a suspension was applied to the dorsal skin. Tumors did not develop at the site of administration in any group. Tumors developed, however, in 29/165 animals that survived until tumor development; 7 animals had tumors at different sites. In Group I, 9/43 animals developed tumors; 6 of these were hepatomas, 1 was a hepatic mixed structure tumor, 3 were adrenal tumors, 1 was of the forestomach, 1 was of the uterus and ovaries, 1 was a melanoma and 1 was of the large intestine. In Group IIa, tumors developed in 4/21 animals: 1 hepatoma, 2 of the uterus and ovaries and 1 benign tumor of the skin. Tumors developed in 13/36 Group IIb animals: 2 hepatomas, 1 hemangioendothelioma and 1 cholangioma of the liver, hepatic mixed structure, 3 adrenal, 4 of the forestomach, 1 of the uterus and ovaries, 1 of the pancreas and 1 benign tumor of the skin. In Group IV, tumors developed in 3/9 animals: 1 lymphangioendothelioma of the liver, 1 adrenal, and 1 forestomach tumor. No tumors developed in Group III. The histological changes are noted. It is concluded that nas is a weak carcinogen. (36 refs.)

77-4974 **Nucleoli of Thioacetamide-treated Liver as a Model for Studying Regulation of the Preribosomal RNA Synthesis.** (Eng.) Andersen, M. W. (Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX 77030); Ballal, N. R.; Busch, H. *Biochem Biophys Res Commun* 78(1): 129-135; 1977.

Liver nucleoli from thioacetamide (TA)-treated male Sprague-Dawley rats had a 5-fold increase in activity within 24 hr following a single injection (50 mg/kg). This increase in activity was maintained with daily injections of TA for 3 days, after which time there was a 7-fold increase in the activity of "free" enzyme. Thus, the increase in endogenous activity parallels an increase in the unbound RNA polymerase I activity. (16 refs.)

77-4975 **Modification of Ribonucleic Acid by Vitamin B$_6$. Specific Interaction of Pyridoxal 5'-Phosphate with Transfer Ribonucleic Acid.** (Eng) Kopelovich, L. (Dept. Molecular Biology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021); Wolfe, G. *Biochemistry* 16(16) 3721-3726; 1977.

The interaction of vitamin B$_6$, in the form of pyridoxal 5'-phosphate (PLP), with transfer RNA (tRNA) was investigated using whole tRNA from a human cell line (HT-29) of colon carcinoma and from *Escherichia coli*. After a 30-min incubation period, samples were reduced by successive additions of sodium borohydride and digested with RNase A and snake venom phosphodiesterase. Two-dimensional chromatography of the PLP-treated tRNA digest showed that PLP bound specifically to GMP. The reaction of PLP with whole tRNA was competitively inhibited by N-acetoxy-2-acetylaminofluorene (N-acetoxy-AAF), suggesting that binding occurred primarily to the G$_{20}$ base residue at the unpaired region of the dihydrouridine loop. Modification of tRNA by PLP resulted in the inhibition, to varying extents, of amino acid acceptance in the aminoacyl-tRNA synthetase assay (10%-80%). Defects in codon recognition by PLP-modified amino acid-acylated tRNA's in the presence of the corresponding guanine-containing polynucleotide triplets were observed by the ribosomal binding assay. These results suggest that translation may be modulated, in part, by interaction of PLP with tRNA. (33 refs.)

77-4976 **Effects of Varying the Onset and Duration of Exposure to Phenobarbital on Its Enhancement of 2-Acetylaminofluorene-induced Hepatic Tumorigenesis.** (Eng) Peraino, C. (Div. Biological and Medical Res., Argonne Natl. Lab., Argonne, IL 60439); Fry, R. J.; Staffeldt, E. *Cancer Res* 37(10): 3623-3627; 1977.

In previous experiments, a phenobarbital-containing diet markedly accelerated the onset and incidence of hepatic tumors induced in Sprague-Dawley rats fed a low concentration of 2-acetylaminofluorene (AAF). The present study examined the characteristics of this interaction between the effects of AAF (0.02% for 18 days) and phenobarbital (PB: 0.05%) by measuring tumor production after changing either the duration of the interval between AAF and PB treatments or the duration of the post-AAF exposure to PB. When AAF and PB treatments were separated by increasing intervals (up to 120 days), the resultant levels of tumor enhancement appeared to be influenced mainly by the duration of the post-AAF PB treatment rather than by the length of the treatment-free interval. Progressive increases in the duration of the PB treatment (begun within 7 days of the AAF treatment) advanced the time at which tumor enhancement occurred and similarly increased the overall tumor incidence. The latter enhancement effects occurred and were sustained after the cessation of the PB treatments. The results of this study suggest that (1) the tumorigenic changes induced by brief AAF treatment are persistent, although the question of their permanence remains open, and (2) PB treatment produces irreversible changes in AAF-modified cells, which lead to the expression of the tumor phenotype. (14 refs.)

77-4977 **Development and Characterization of a Tumorigenic Mouse Urinary Bladder Cell Line Induced by 2-Acetylaminofluorene (Meeting Abstract).** (Eng) Berky, J. J. (National Center for Toxicological Research, Jefferson, AR 72079); Zolotor, L. *In Vitro* 13(3): 165; 1977. (no refs.)

77-4978 **Evolution of the Hepatocyte Population in the Process of Chemical Carcinogenesis.** (Rus) Bannikov, G. A. (Lab. Mechanisms Carcinogenesis, Oncological Res. Center, USSR Acad. Medical Sciences, Moscow, USSR); Gel'shtein, V. I.; Chipysheva, T. A. *Vopr Onkol* 23(4): 39-44; 1977.

Hepatocyte changes in random-bred male albino rats fed either 3′-methyl-4-dimethylaminoazobenzene (DAB) or 2-acetylaminofluorene (AAF) were investigated. Rats receiving DAB were fed a modified Miller diet containing 0.06% of the carcinogen; rats fed AAF were given a Miller diet for 11 days, 0.06% AAF for 7 days, Miller diet for 7 days, 0.06% AAF for 21 days and a Miller diet for 7 days. Alpha-fetoprotein was a marker of embryonic hepatocyte differentiation, and ligandin served as a marker of differentiated mature hepatocytes. The toxic effect on stem cells was accompanied by a decrease in ligandin content in centrilobar hepatocytes. Among newly proliferating elements, 'oval' cells, cells of the bile tract epithelium, and most of the basophilic hepatocyte-like cells contained neither alpha-fetoprotein nor ligandin. Small groups of basophilic hepatocyte-like cells contained alpha-fetoprotein. Ligandin was found in columnar epithelium similar to that of the intestine, but alpha-fetoprotein was absent. Alpha-fetoprotein was also absent in oxyphilous hepatocytes of hyperplastic nodules. Nodules contained either no ligandin, normal amounts or high amounts (hyperdifferentiated cells); within one nodule, all cells had identical ligandin content. It is believed that these multiple foci of differentiation are necessary for tumor evolution. (21 refs.)

77-4979 **Carcinogenicity of 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (AF-2) Fed to Female Sprague-Dawley Rats.** (Eng) Cohen, S. M. (First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan); Ichikawa, M.; Bryan, G. T. *Gann* 68(4): 473-476; 1977.

In acute toxicity tests, doses of 0.05%, 0.1%, and 0.2% 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide (AF-2) were administered in the diet to female Sprague-Dawley rats. No symptoms of acute toxicity were noted at any dose, and no tissue abnormalities were detected by light microscopy. In chronic studies, AF-2 was administered at 0.2% by wt in the diet for 46 wk; a control diet was then given for 20 wk, and the rats were autopsied at death. AF-2-fed animals had a mean survival of 52 wk compared to 65 wk for controls. The first mammary tumor was noted during the 24th wk of the experiment but most were not palpated for more than 1 yr after feeding had begun. Twenty-four of 29 rats fed AF-2 developed breast tumors (15 adenocarcinomas and 9 fibroadenomas); 17 tumors were solitary, and the remainder were multiple. The adenocarcinomas had a mean latent period of 50 wk, while that for fibroadenomas was 60 wk. Two rats fed AF-2 also developed uterine myxomas, and one developed an ovarian follicular cyst; one also had a unilateral calculus of the renal pelvis with severe hyperplasia of the pelvic urothelium. (27 refs.)

77-4980 **Mutagenicity of Furylfuramide, a Food Preservative, Tested by Using Alanine-requiring Mouse L5178Y Cells In Vitro and In Vivo.** (Eng) Nakamura, N. (Dept. Radiation Biophysics, Faculty Medicine, Univ. Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo, Japan); Suzuki, N.; Okada, S. *Mutat Res* 46(5): 355-364; 1977.

The mutagenicity of furylfuramide (FF) was tested by a reversion assay in alananine-requiring mouse L5178Y cells (Ala 32 cells) and by a host-mediated assay in BDF_1 mice. No significant increase in mutation occurred in Ala 32 cells exposed to up to 50 μg/ml FF, nor was FF mutagenicity detected in the host-mediated assay, in which mice were fed drinking water containing 20 or 100 μg/ml FF or inoculated iv with 40 μg/g FF. When added to the in vitro assay system at optimal concentration, a hepatic microsomal fraction (S-9), prepared from phenobarbital-treated rats, inhibited cell growth and increased cell killing and mutagenesis. The failure of the reversion system without S-9 to detect mutagenicity in FF was attributed to a deficiency of the FF-activating enzyme system(s) in mouse L5178Y cells. Based on the mutation frequencies in the presence of the S-9 mixture, 10 μg FF was equal to a 150 rec (rem-equivalent-chemicals) unit in the reversion assay and in an assay of methotrexate-sensitive cells. An estimate is given of the annual genetic load to the Japanese population. (21 refs.)

77-4981 **Structure of a Dinucleoside Phosphate-Drug Complex as Model for Nucleic Acid-Drug Interaction.** (Eng) Neidle, S. (Dept. Biophysics, Univ. London King's Coll., 26-29 Drury Lane, London WC2, England); Achari, A.; Taylor, G. L.; Berman, H. M.; Carrell, H. L.; Glusker, J. P.; Stallings, W. C. *Nature* 269(5626): 304-307; 1977.

The crystal structure of a 3:2 complex between the mutagen proflavine and the dinucleoside phosphate cytidylyl-3′,5′ guanosine was determined in the hope that it would serve as a model for proflavine-nucleic acid interactions. The complex contains one drug molecule intercalated between Watson-Crick base pairs of the nucleotide duplex, and the other two proflavine molecules are bound to the exterior of the miniature double helix. The similarity of the orientation of the overlapping base pair planes to those in RNA 11 implies that proflavine does not unwind the helix. (28 refs.)

77-4982 **Enhancement of Mammary Tumor Formation in Mice by a Cytostatic Drug, Melphalan.** (Eng.) Medina, D. (Dept. Cell Biology, Baylor Coll. Medicine, Houston, TX 77030). *Cancer Res* 37(1): 317-319; 1977.

Melphalan, injected ip in doses of either 2.5 or 5.0 mg/kg to female Balb/c mice, markedly enhanced tumor formation in the preneoplastic hyperplastic alveolar nodule mammary outgrowth line D2. (16 refs.)

77-4983 **Enhancement and Inhibition of Mammary Tumor Formation and Growth by Cytostatic Drugs.** (Eng) Medina, D. (Dept. Cell Biology, Baylor Coll. Medicine, Houston, TX 77030); Shepherd, F. *Cancer Res* 37(10): 3571-3577; 1977.

The effects of L-phenylalanine mustard (L-PAM), methotrexate (MTX), 5-fluorouracil (5-FU), cyclophosphamide (CP), vincristine (VC), and prednisone (PD) on preneoplastic mammary growth and tumorigenesis were examined in BALB/c mice bearing preneoplastic, hyperplastic alveolar nodule outgrowth lines D2 and C4. High doses of L-PAM, CP, and 5-FU inhibited nodule growth rate in the mammary fat pads for both nodule lines. For nodule line D2, L-PAM, 5-FU, CP, and VC enhanced and MTX and PD inhibited the rate of tumor formation. For nodule line C4, VC enhanced and 5-FU, CP, MTX, and PD inhibited the tumor formation rate. L-PAM had no effect for line C4. There was no correlation between the effect of a drug on nodule growth and its effect on tumor formation. In contrast, L-PAM, 5-FU, CP, and MTX inhibited the growth of sc transplanted tumors derived from both nodule lines. These results suggest that preneoplastic mammary populations respond differently from neoplastic mammary populations to the same cytostatic drugs and that some cytostatic drugs can promote mammary tumorigenesis. (25 refs.)

77-4984 **Phenylpentylisatins: A Novel Class of Alkaloids from *Melochia tomentosa*.** (Eng.) Kapadia, G. J. (Dept. Biomedicinal Chemistry, Coll. Pharmacy and Pharmacal Sciences, Howard Univ., Washington, DC 20059) Shukla, Y. N.; Chowdhury, B. K.; Basak, S. P.; Fales, H. M.; Sokoloski, E. A. *J Chem Soc [Chem Comm]* 15: 535-536; 1977.

The structures of two alkaloids of the tumorigenic plant, *Melochia tomentosa*, were characterized as 6,7-dimethoxy-4-(5-phenylpentyl)isatin and 4-(5-phenylpentyl)isatin. (6 refs.)

77-4985 **Effect of N-(3,5-Dichlorophenyl)succinimide on the Histological Pattern and Incidence of Kidney Tumors Induced by Streptozotocin in Rats.** (Eng) Shinohara, Y. (First Dept. Pathology, Nagoya Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-kuk Nagoya 467, Japan); Miyata, Y.; Murasaki, G.; Nakanishi, K.; Yoshimura, T.; Ito, N. *Gann* 68(4): 397-404; 1977.

The effect of N-(3,5-dichlorophenyl)succinimide (NDPS) on the histological pattern and incidence of kidney tumors induced by streptozotocin in male Sprague-Dawley rats was investigated. The first group of rats received a single dose of streptozotocin (65 mg/kg) iv and was then fed stock for 40 wk. In group 2, streptozotocin (65 mg/kg) was administered iv on day 1, rats were fed stock for 2 wk, a diet containing 0.5% NDPS for 8 wk, and stock for 30 wk. In group 3, rats were given 65 mg/kg streptozotocin iv and two doses of nicotinamide (350 mg/kg) ip followed by 40 wk of stock diet. In group 4, rats received two doses of nicotinamide (350 mg/kg) ip on day 1 and 40 wk of stock. Group 5 served as control. In groups 1 and 2, the body wt increased compared with controls and a slight increase in liver wt was noted. There was a slight increased in SGOT and SGPT in the blood of animals fed streptozotocin. Ten tumors were found in rats treated with the antibiotic alone or combined with NDPS or nicotinamide; two of these developed in the same kidney of one group 2 animal. The tumors occurred in the renal cortex and frequently extended into the medulla; further invasive growth was not noted. Seven were renal cell tumors (groups 1, 2, and 3) and three were embryonal cell tumors (group 2 only); their histology is presented. Renal cell tumors were induced more frequently in rats fed NDPS. Nicotinamide had no effect on carcinogenesis. Three of 9 rats in group 1 and 11/17 rats in group 3 also developed islet cell pancreatic tumors; this histology is presented. These findings suggest a direct tumorigenic action of streptozotocin on the kidneys unrelated to its diabetogenic effect. (26 refs.)

77-4986 **Effect of Urethane on Swiss Mice Lung Tissue in Organ Culture and Proliferation of Epithelial Cells 'In Vitro'.** (Eng) Ranade, J. P. (Biology Div., Cancer Res. Inst., Parel, Bombay-400 012, India); Bapat, C. V.; Ranadive, K. J. *Indian J Cancer* 14(2): 136-140; 1977.

The early effects of urethane were studied in vitro using 1-day-old Swiss mice lung tissue cells. The lung tissues were organ cultured with and without urethane (10 mg/ml) for 24 hr. Explants were trypsinized, and the cells were plated for monolayer culture. Discrete epithelial and fibroblast colonies developed that were counted by number and size. The colony and area counts indicated that urethane-treated cultures produced 50% more epithelial cells. There was a 2.8-fold decrease in the number of mitotic fibroblasts and a 3-fold increase in the number of mitotic epithelial cells in treated cultures compared to controls. These results indicate that urethane promotes the proliferation of epithelial cells and that it may be toxic to fibroblasts. Epithelial cell proliferation in the urethane-treated cultures may be the first step toward adenoma development. (27 refs.)

77-4987 **Tumors and Amyloidosis in Mice Painted with Crude Oil Found on Bathing Beaches.** (Eng) Barr-Nea, L. (Dept. Histology and Cell Biology, Sheba Medical Center, Tel-Hashomer, Israel); Wolman, M. *Bull Environ Contam Toxicol* 18(3): 385-391; 1977.

Lumps of crude oil (from tanker spillage) collected on Israeli beaches in 1970, 1971, and 1973 were extracted with acetone and topically applied to the skin of random-bred male ICR mice twice weekly for 12 mo. The results show that 3/22 animals painted with 1970 oil developed tumors, one skin papilloma and two reticulum cell sarcomas. One skin papilloma was found in the skin of a mouse painted with 1971 oil. No tumors were found in the 1973 oil-painted animals. Mice painted with acetone alone for 12 mo developed amyloidosis to a similar extent (12/23) as those painted with the oldest oil (10/22). Painting with the 1973 oil produced amyloidosis in only a few animals (2/12), indicating that aging of the oils may be the main factor in their pathogenesis. The possibility is raised that acetone and oil may act synergistically or be antagonistic at different stages of aging and amyloidogenesis. (3 refs.)

77-4988 **Use of Hair Dyes by Patients with Breast Cancer: A Case-Control Study.** (Eng.) Kinlen, L. J. (DHSS Cancer Epidemiology and Clinical Trials Unit, Dept. Regius Professor Medicine, Univ. Oxford, Oxford, England) Harris, R.; Garrod, A.; Rodriguez, K. *Br Med J* 2(6083): 366-368; 1977.

The use of hair dye preparations before the diagnosis of cancer was studied in 191 women with breast cancer and 561 matched controls who did not have malignant disease. The results revealed no significant difference in the use of hair dyes between the groups. Further epidemiological studies are necessary. (9 refs.)

77-4989 **Cytological Effects of Insecticides on a Human Lymphoblastoid Cell Line (Meeting Abstract).** (Eng) Trepanier, G. (Institut Armand-Frappier, Laval-des-Rapides, Quebec, Canada H7N 4Z3); Marchessault, F.; Bansal, J.; Chagnon, A. *In Vitro* 13(3): 201; 1977. (no refs.)

77-4990 **Squamous Cell Carcinoma of the Buccal Mucosa Associated with Chronic Oral Polyvinyl Chloride Exposure. Report of a Case.** (Eng.) Casterline, C. L. (Box #191, Walter Reed Army Medical Center, Washington, DC 20012); Casterline, P. F.; Jaques, D. A. *Cancer* 39(4): 1686-1688; 1977.

A case is reported of a 22-yr-old man who developed squamous cell carcinoma of the buccal mucosa. He had acquired the habit of chewing and storing plastic materials containing polyvinyl chloride in his mouth for up to 8 hr/day since his childhood. The only family history of cancer was breast cancer in his maternal grandmother. (9 refs.)

77-4991 **Irreversible Binding of ^{14}C-labelled Trichloroethylene to Mice Liver Constituents in Vivo and in Vitro.** (Eng.) Uehleke, H. (Bundesgesundheitsamt, Abteilung Toxikologie, D-1000 Berlin 33, W. Germany); Poplawski-Tabarelli, S. *Arch Toxicol (Berl)* 37(4): 289-294; 1977.

^{14}C-labeled trichloroethylene (10 μmoles/g) administered to male NMRI mice resulted in irreversible binding to the protein of liver fractions. After oral or ip doses of undiluted trichloroethylene, peak liver concentrations were found between 60 and 90 min, with only slightly higher concentrations after ip injection. Covalent binding increased two-fold in microsomes of mice pretreated with phenobarbital. (20 refs.)

77-4992 **Rat Liver Changes after Subchronic Exposition to Polychlorinated Biphenyls (PCB) of Low Chlorine Content.** (Eng) Schmoldt, A. (Dept. Pharmacology, Martinistr. 52, D-2000 Hamburg 20, W. Germany); Altenahr, E.; Grote, W.; Dammann, H. G.; Sidau, B.; Benthe, H. F. *Arch Toxicol* 37(3): 203-217; 1977.

A commercial polychlorinated biphenyl (PCB) mixture, Clophen A30 with 42% chlorine [trichlorobiphenyl (triCB-5)], and two purified products with 2% and 0.4% highly chlorinated biphenyls (triCB-2 and triCB-0.4, respectively) were administered in subchronic doses to male Wistar rats and the liver changes examined. The animals received the PCBs at 2000 ppm in the diet for 12 wk. The body wt of the PCB-treated rats was reduced, but the liver wt was increased; the general structure of the liver was preserved, however. The most noticeable effect, apparent in all animals, was cytoplasmic clumping and the occurrence of annular inclusion bodies in the cytoplasm. Electron microscopy revealed a proliferation of the tubular and vesicular smooth endoplasmic reticulum (SER). Mitochondria were also displaced but most were intact; however, in two rats exposed to triCB-5 for 9 wk, hydropically swollen and bizarrely shaped mitochondria were noted. In acute experiments with 1.7 millimole/kg diCB, tetraCB or hexaCB, it was noted that the increased liver wt was due to cell hypertrophy. After subchronic exposure, SGOT and SGPT activities were normal, but plasma elimination of sulfobromophthalein was increased; elevated phospholipid values correlated with SER proliferation. triCB-5 produced the highest induction of the microsomal monooxygenases, but the other effects of the triCBs were equal. Porphyria induction by all compounds was probably due to decarboxylation inhibition. The content of triCB-5 in the livers exceeded that of the other two triCBs but the difference was not significant. It is concluded that low chlorinated PCBs have a lower hepatotoxicity than those with high chlorine content. (31 refs.)

77-4993 **Enhanced Polychlorinated Biphenyl Lesions in Moloney Leukemia Virus-infected Mice.** (Eng.) Koller, L. D. (Sch. Veterinary Medicine-Oregon State Univ., Corvallis, OR 97331). *Clin Toxicol* 11(1): 107-116; 1977.

This study was made to determine if different formulations of polychlorinated biphenyls (PCB) affect the induction of neoplasia by Moloney leukemia virus (MLV) or if MLV affects the toxicity of PCB. PCB's are hepatotoxic, and neoplasia produced by MLV may involve the liver. Hepatic toxicity produced by a 6-mo exposure to the PCB Aroclors 1254 and 1242 was enhanced by MLV; Aroclor 1254 caused death before 6 mo. Aroclor 1221 did not affect the mice. Liver wts corresponded with the dose of PCB given (375, 37.5, or 3.75 ppm in the diet). Liver wts of mice that were removed from the PCB feed at 6 mo and then fed a PCB-free diet for an additional 3 mo decreased in size and were similar to those of non-PCB-exposed mice. The results showed that an oncogenic virus (MLV) enhanced PCB-induced hepatic toxicity, but, conversely, the PCB's did not activate MLV. (22 refs.)

77-4994 **Metabolism In Vivo of Dioxane: Effect of Inducers and Inhibitors of Hepatic Mixed-Function Oxidases.** (Eng.) Woo, Y. (Seamen's Memorial Res. Lab., USPHS Hosp., 210 State St., New Orleans, LA 70118); Argus, M. F.; Arcos, J. C. *Biochem Pharmacol* 26(16): 1539-1542; 1977.

To investigate the involvement of mixed-function oxidases (MFO) in the in vivo metabolism of dioxane, their effect on the excretion of p-dioxane-2-one was studied in male Sprague-Dawley rats. Dioxane (3 g/kg) was given ip. Three typical inducers of MFO were employed: phenobarbital (PB), polychlorinated biphenyls (PCB), and 3-methylcholanthrene (MC). PB increased the total amount of p-dioxane-2-one excreted significantly. The time required for peak excretion was reduced from 20-28 hr for control rats to 12 hr for PB-treated rats. Similar results were obtained with PCB, but MC had no effect. All these results strongly support the involvement of microsomal MFO in the in vivo metabolism of dioxane. 2,4-Dichloro-phenylphenoxyethylamine, a potent long-acting inhibitor of MFO, inhibited the excretion of p-dioxane-2-one from untreated and PB- and PCB-treated rats, and cobaltous chloride, a repressor of cytochrome P-450 synthesis, also inhibited the metabolite excretion. (10 refs.)

77-4995 **Metabolism In Vivo of Dioxane: Identification of p-Dioxane-2-one as the Major Urinary Metabolite.** (Eng.) Woo, Y. (Seamen's Memorial Res. Lab., USPHS Hosp., 210 State St., New Orleans, LA 70118); Arcos, J. C.; Argus, M. F.; Griffin, G. W.; Nishiyama, K. *Biochem Pharmacol* 26(16): 1535-1538; 1977.

To determine the mechanism of the carcinogenic action of p-dioxane, its metabolism in vivo was studied in Sprague-Dawley rats given the compound ip (50-400 mg/100 g). Urine samples were taken and a metabolite was recovered. Administration of diethylene glycol gave the same metabolite. Infrared spectrometry, nuclear magnetic resonance spectrometry, and gas chromatography-mass spectrometry identified the metabolite as p-dioxane-2-one. The possible metabolic pathways of dioxane are discussed and shown schematically. (12 refs.)

77-4996 **Chromosome Aberrations and Sister-Chromatid Exchange in Workers in Chemical Laboratories and a Rotoprinting Factory and in Children of Women Laboratory Workers.** (Eng) Funes-Cravioto, F. (Dept. Clinical Genetics, Karolinska Hosp., S-104 01 Stockholm 60, Sweden); Kolmodin-Hedman, B.; Lindsten, J.; Nordenskjold, M.; Zapata-Gayon, C.; Lambert, B.; Norberg, E.; Olin, R. *Lancet* 2(8033): 322-325; 1977.

Chromosome aberrations were studied in the lymphocytes of 73 apparently healthy workers in chemical laboratories and a printing factory, 14 children (4 days - 11 yr old) whose mothers worked in the laboratories while pregnant, and of 49 control subjects (42 adults and 7 children). All of the laboratory and printing workers had been exposed to various organic solvents (benzene, toluene, chloroform, xylene, tetrahydrofuran, methanol, cyclohexane, diethyl ether). Lymphocytes from the exposed subjects had a significantly increased frequency of chromatid and isochromatic breaks in comparison with the control group. There was also a significant increase in the number of chromosome aberrations in the children of exposed mothers compared to control children. A significant correlation between age and frequency of chromosome aberrations was seen for exposed and control children, but not for adults. The incidence of sister-chromatid exchange was significantly increased in 12 technicians performing hormone analyses; 4 children of 2 female technicians working during pregnancy also had a significantly increased frequency of sister-chromatid exchange. Those who had been exposed most heavily to organic solvents did not necessarily have the highest frequency of cytogenetic changes. There was a low correlation between the frequency of chromosome breaks and the number of years of exposure. It is suggested that an equilibrium between the degree of exposure, cell turnover, and the degree of damage may be reached with time in the exposed groups. (18 refs.)

77-4997 **DNA Damage and Repair by Alkaline Elution in N-Diazoacetylglycine Amide-treated Cells.** (Eng) Cavanna, M. (Inst. Pharmacology, Genoa Univ., Viale Benedetto XV, 2, 16132-Genoa, Italy); Parodi, S.; Sciaba, L.; Maura, A.; Carlo, P.; Cajelli, E.; Brambilla, G. *Toxicol Lett* 1(2): 115-120; 1977.

The alkaline elution technique was used to assess DNA damage and repair in 18BcR fibroblast-like cells from the kidneys of BALB/c mice following treatment with N-diazoacetylglycine amide (DGA). Dose-dependent DNA damage was evident after treatment of cells with doses ranging from 10 to 0.31 mM. Five days after 10 mM DGA treatment, a 50% reduction was noted in treated cells. Treatment of cells with 5 mM DGA for 1 hr revealed that the damaging effect did not stop after challenge and in fact increased for 2 more hr; it then regressed after 4 to 24 hr of repair. These findings are in agreement with the carcinogenic and mutagenic data on DGA. This technique could be used for the rapid screening of environmental carcinogens. (12 refs.)

77-4998 **Tumors Following Experimental Lithiasic Cholecystitis, with or Without Added Carcinogens, in Mice.** (Fre) Besancon, F. (Clinique et Semiologie Medicales, Hotel-Dieu, Parvis Notre Dame, 75004 Paris, France); Marche, C.; Habar, J. L.; Parrot, J.; Damianakis, N. *Ann Gastroenterol Hepatol (Paris)* 13(3): 195-207; 1977.

The effects of a diet containing 5% sodium dehydrocholate (SD) were investigated in two strains of C57 black mice with liver tumors induced by 2-amino-5-azotoluene (AAT: 10 mg sc, C57BL mice), aramite (AM: 0.01 ml sc, C57BL mice) and isoniazid (2 mg daily po, C3HeB mice). The animals were sacrificed 15 to 18 mo after the start of the experiment, and the gallbladder and liver were examined microscopically. In C57BL mice, SD consistently induced gallstones together with chronic hyperplastic and diverticular cholecystitis, but C3HeB mice were resistant to lithiasis and the different lesions. The frequency of adenomatous hyperplasia (similar to human oncocytic metaplasia) of the gallbladder was greatest in animals treated with SD + AAT (60%), SD + AM (58%), and AM alone (40%). A significant increase in hepatomas was seen in animals given SD (7/13 mice: $p < 0.001$). The incidence of hepatomas was small compared to the incidence induced by AAT: a 100% and a 97% incidence of hepatomas was seen in C57BL mice given SD + AAT and AAT alone, respectively. Only a 15% incidence was noted with AM alone, but this increased to 51% following addition of SD. AAT and AM induced no biliary cancers stricto sensu in C57BL mice. Isoniazid had no effect on C3HeB mice, the only strain tested. The study suggests that chronic inflammation in the bile ducts and other organs may be a preneoplastic state. (26 refs.)

77-4999 **Correlation of Bacterial Mutagenicity and Hamster Cell Transformation with Tumorigenicity Induced by 2,4-Toluenediamine.** (Eng.) Pienta, R. J. (Chemical Carcinogenesis Program, NCI, Frederick Cancer Res. Center, Frederick, MD 21701) Shah, M. J.; Lebherz, W. B.; Andrews, A. W. *Cancer Lett* 3(1/2): 45-52; 1977.

In the presence of rat liver microsome enzymes, 2,4-toluenediamine (TDA) was mutagenic for *Salmonella typhimurium* tester strains TA 1538 and TA 98. At 0.5 μg/ml, TDA induced morphological transformation in an in vitro carcinogenesis system using secondary culture target cells prepared from cryopreserved primary Syrian hamster embryo cells. These results correlate bacterial mutagenicity and in vitro morphological transformation with the reported tumorigenicity of this compound. (23 refs.)

77-5000 **Non-epithelial Uterine Tumours Induced in CBA Mice by 1,2-Dimethylhydrazine.** (Eng) Turusov, V. S. (Cancer Res. Centre USSR Acad. Medical Sciences, Kashirskoye Shosse, 6, Moscow, USSR); Bazlova, L. S.; Lanko, N. S. *Cancer Letter* 3(1-2): 37-44; 1977.

A high incidence of uterine sarcoma was induced in CBA mice upon administration of 1,2-dimethylhydrazine (DMH) sc at a dose of 8 mg/kg once a week for 38-40 wk. The first tumor was found at 29 wk; and in all, 28 tumors developed in 43 mice. Histologically, most of the tumors were considered mesenchymal tumors, or endometrial sarcomas. There was no evidence of metastasis, but the tumors were obviously malignant, as confirmed by their structural and cellular polymorphism, the high number of mitoses, and the rapidity with which they grew upon transplantation. They always involved the uterine body or horns, and not only the parametrium; the uterine horns were usually diffusely thickened and firm, with no discernible lumen. In only a few hemorrhagic areas could the presence of a vascular tumor be suspected. The histogenesis of these tumors is also discussed. (10 refs.)

77-5001 **Tumorigenic Effect of 4-Methylphenylhydrazine Hydrochloride in Swiss Mice.** (Eng.) Toth, B. (Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, Omaha, NB 68105); Tompa, A.; Patil, K. *Z Krebsforsch* 89(3): 245-252; 1977.

The tumor-inducing ability of 4-methylphenylhydrazine hydrochloride (4-MPH) was studied in Swiss mice. The compound was given in 10 weekly sc injections of 140 μg/g or as 7 weekly intragastric (ig) installations of 250 μg/g in physiological saline. 4-MPH induced tumors of the lungs and blood vessels in the mice. In those treated sc, the incidence of lung tumors was 36% in females and 44% in males; the corresponding incidence in animals treated ig was 40% in females and 34% in males. In addition, 4-MPH produced blood vessel tumors by the ig route in 32% of the females and 18% of the males; sc, the incidences were 8% and 14%, respectively. Histopathologically, the lesions were adenomas and adenocarcinomas of the lungs and angiomas and angiosarcomas of the blood vessels. 4-MPH was postulated to be a metabolite of 4-hydroxymethylphenylhydrazine, an ingredient of the commonly eaten mushroom *Agaricus bisporus*. (17 refs.)

77-5002 **The Mutational Spectrum of Procarbazine in *Drosophila melanogaster*.** (Eng) Blijleven, W. G. (Dept. Radiation Genetics and Chemical Mutagenesis, Sylvius Lab., State Univ. Leiden, Wassenaarseweg 72, Leiden, Netherlands); Vogel, E. *Mutat Res* 45(1): 47-59; 1977.

The mutagenic activity of procarbazine was examined in *Drosophila melanogaster*. Recessive lethal mutations were noted in all stages of spermatogenesis. At low concentrations there was a clear-cut concentration-effect relationship in spermatids; at high concentrations, the induction of recessive lethals was not a function of concentration. There was no observed partial sex-chromosome loss or II-III translocations. (29 refs.)

77-5003 **Urinary Tract Cancer and Isoniazid.** (Eng) Glassroth, J. L. (Res. and Development Branch, Tuberculosis Control Div., Center Disease Control, Atlanta, GA 30333); Snider, D. E.; Comstock, G. W. *Am Rev Respir Dis* 116(2): 331-33[illegible] 1977.

The possibility that isoniazid (INH) might be associated with the development of urinary tract cancer was investigated in Washington County, MD. Approx 500 cases of tuberculosis (TB) have been reported in this area in the past 25 yr, and INH has been used for the past 15 yr for certain high-risk groups (tuberculosis contacts, dormant cases, etc). Cases for this study consisted of all persons with bladder cancer (142) or renal cancer (48) who were found in the follow-up of a 1963 census population. Each case was matched (by sex, race, and age) to two other persons listed in the census. The TB registry was searched to determine whether any case or control had ever taken INH. Only two members of the entire study group had a record of INH administration, both controls. There was no evidence that INH contributes to the production of urinary cancer in man. (13 refs.)

77-5004 **Morphology of Mammary Gland, Ovaries, and Pituitary Gland of Hydroxylamine-fed C3H/HeN Mice.** (Eng.) Evarts, R. P. (Building 37, Room 3B27, NCI, NIH, Bethesda, MD 20014); Brown, C. A. *Lab Invest* 37(1): 53-63; 1977.

In five separate experiments, 218 nulliparous female C3H/HeN mice were given hydroxylamine sulfate (HS) in their drinking water as a 10 mM solution. HS clearly retarded development of the mammary glands and ovaries when administration started at the age of 6 wk. Among the test animals, the number of hyperplastic nodules remained lower and mammary tumor frequency was reduced (31% vs 100% in controls). HS was still effective in preventing tumors, preventing formation of corpora lutea, and increasing the number of follicles when given at the age of 13 wk. When started at the ages of 18, 24, and 28 wk, ductular development was not affected but ovaries still showed morphological changes. At the age of about 6 mo, HS seemed to increase rather than decrease tumor frequency. A hormonal imbalance may be produced that affects pituitary and/or hypothalamus function. The occurrence of pseudopregnancies and numerous corpora lutea in controls suggests significant progesterone production, which may enhance carcinogenesis, whereas the opposite was found in mice fed HS. (20 refs.)

77-5005 **Comparative Mutagenesis of Quinolines.** (Eng.) Epler, J. L. (Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830) Winton, W.; Ho, T.; Larimer, F. W.; Rao, T. K.; Hardigree, A. A. *Mutat Res* 39(3/4): 285-296; 1977.

Quinoline, 8-hydroxyquinoline, 8-nitroquinoline, and 8-aminoquinoline were tested for mutagenicity in *Salmonella typhimurium Saccharomyces cerevisiae* human WBC and *Drosophila melanogaster*. The demonstration of mutagenicity of these quinolines suggests that they may be potential carcinogenic agents. (27 refs.)

77-5006 **Rapid Production of Hyperplastic Liver Nodules in Rats Treated with Carcinogenic Chemicals: A New Approach for an In Vivo Short-term Screening Test for Hepatocarcinogens.** (Eng) Tatematsu, M. (First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan); Shirai, T.; Tsuda, H.; Miyata, Y.; Shinohara, Y.; Ito, N. *Gann* 68(4): 499-507; 1977.

A method for the rapid induction of hyperplastic liver nodules in male Sprague-Dawley rats was tested. The rats were first injected ip with 200 mg/kg diethylnitrosamine (DEN) and maintained on a basal diet for 2 wk; 2 wk later, either N-2-fluorenyl-acetamide (2-FAA; 0.02%), 3′-methyl-4-(dimethylamino)azobenzene (3′-Me-DAB; 0.06%), dimethylnitrosamine (DMN; 0.01%), DEN (0.05%), DL-ethionine (0.25%), quinoline (0.25%), 5,7-bromo-8-hydroxyquinoline (0.25%), 8-hydroquinoline (0.50%) or 8-nitroquinoline (0.10%) in the diet was administered for 2 wk. Partial hepatectomy was then performed after 3 wk, and the rats were killed after 4 wk. Significant differences in the number of hyperplastic nodules were found among animals fed 2-FAA, 3′-MeDAB, DEN, DMN, DL-ethionine and quinoline. These differences were not noted when partial hepatectomy was not performed, nor when the chemicals were administered continuously for 4 wk with or without partial hepatectomy.γ-Glutamyltranspeptidase activity was present in hyperplastic nodules and in the epithelium of the bile duct and portal ducts, but was absent in non-hyperplastic areas. Acid phosphatase, glucose-6-phosphatase, and ATPase were present in the non-hyperplastic tissues but were low in the hyperplastic nodules. Alkaline phosphatase activity was poorly defined in hyperplastic nodules and normal parenchyma. This procedure represents a potentially useful system for the in vivo evaluation of hepatocarcinogenicity. (41 refs.)

77-5007 Macromolecular Complexes Produced by Chemical Carcinogens and Ultraviolet Radiation. (Eng) Morin, N. R. (Div. Neurosurgery, Univ. Wisconsin Sch. Medicine, Madison, WI 53706); Zeldin, P. E.; Kubinski, Z. O.; Bhattacharva, P. K.; Kubinski, H. *Cancer Res* 37(10): 3802-3814; 1977.

The effects of several carcinogenic and noncarcinogenic chemicals, UV light, and some presumably noncarcinogenic analogs of carcinogenic compounds were tested for their ability to induce in vitro complexes between purified nucleic acids (NA) and between NA and proteins. All the ultimate tumor-producing agents tested fell into two distinct groups with respect to their ability to form macromolecular complexes. Class A chemicals included several mono- and polyfunctional alkylating agents. Both NA-NA and protein-NA adducts were produced in the presence of these compounds. Class B was exemplified by N-acetoxy-2-acetylaminofluorene (AAF), beryllium salts, and UV light. Complexes between proteins and NA, although not between the NA themselves, were produced in the presence of Class B agents. Nonultimate carcinogenic chemicals such as AAF and 2-acetylaminofluorene did not give rise to macromolecular complexes. However, they could be transformed into apparently active forms that behaved like Class B carcinogens after exposure to mouse or rat liver extracts (postmitochondrial supernatants). No macromolecular complexes were produced by noncarcinogenic chemicals. The data indicate that a significant number and possibly all of the tumor-producing agents are able to form macromolecular complexes. If strong bonds between various chromosomal macromolecules are produced in living cells exposed to carcinogenic agents, one extreme consequence of their formation may be a nondisjunction of daughter chromosomes during mitosis and/or a chromosomal breakdown. Such chromosomal aberrations are believed to correlate with malignant transformation. (59 refs.)

77-5008 Induction of Unscheduled DNA Synthesis by Chemical Mutagens in Testicular Cells of the Mouse In Vitro. (Eng) Beikirch, H. (Zentrallaboratorium fur Mutagenitatsprufung der Deutschen Forschungsgemeinschaft, Breisacher Strasse 33, D-7800 Freiburg i Br., W. Germany). *Arch Toxicol* 37(3): 195-201; 1977.

The ability of 13 test compounds (mostly mutagens) to induce unscheduled DNA synthesis (UDS) in in vitro cultures of mouse testicular homogenates was investigated. Normal replication was suppressed by hydroxyurea, and the compounds were then tested. Methyl methanesulfonate [1×10^{-5} to 2.5×10^{-4} mole/liter (m/l)], ethyl methanesulfonate (1×10^{-3} to 1×10^{-2} m/l), N-methyl-N′-nitro-N-nitrosoguanidine (1×10^{-6} to 1×10^{-5} m/l), triaziquone (5×10^{-8} to 1×10^{-6} m/l), nitrogen mustard (1×10^{-5} to 5×10^{-4} m/l), ICR-191 (5×10^{-7} to 1×10^{-5} m/l), mitomycin C (1×10^{-6} to 1×10^{-4} m/l) and 4-nitroquinoline 1-oxide (1×10^{-7} to 1×10^{-5} m/l) stimulated UDS. 9-Aminoacridine (1×10^{-7} to 1×10^{-4} m/l), hydroxyurethane (1×10^{-6} to 1×10^{-2} m/l), α-naphthylamine (1×10^{-6} to 1×10^{-3} m/l), 2-acetylaminofluorene (1×10^{-7} to 5×10^{-4} m/l) and N-hydroxy-2-acetylaminofluorene (1×10^{-7} to 5×10^{-4} m/l) were ineffective. It should be emphasized, however, that the mixture of different testicular cells used in this system may have had different sensitivities to the compounds tested; different results have been obtained in other test systems (eg, for 2-acetylaminofluorene). This rapid prescreening procedure could be useful for preliminary evaluation of mutagenic and carcinogenic potential. (12 refs.)

77-5009 Inhibition of Testicular DNA Synthesis by Chemical Mutagens and Carcinogens. Preliminary Results in the Validation of a Novel Short Term Test. (Eng) Seiler, J. P. (Swiss Federal Res. Station, CH-8820 Waedenswil, Switzerland). *Mutat Res* 46(4): 305-310; 1977.

The inhibition of testicular DNA synthesis was measured in male mice as an in vivo mammalian screening test for chemical carcinogens and mutagens. Test results for 100 substances indicated that at least 86% of the known carcinogens and/or mutants significantly inhibited thymidine incorporation into testicular DNA compared with only 10% of the noncarcinogenic and nonmutagenic compounds. Furthermore, the assay correctly identified the carcinogenic partner in several pairs of isomeric or otherwise closely related compounds. However, amounts up to the LD50 of the test substances were required to elicit a response. (14 refs.)

77-5010 **Uncertainty Estimates for Low-Dose-Rate Extrapolations of Animal Carcinogenicity Data.** (Eng) Guess, H. (Natl. Inst. Environmental Health Sciences, NIH, Research Triangle Park, NC 27709); Crump, K.; Peto, R. *Cancer Res* 37(10): 3475-3483; 1977.

The statistical uncertainty associated with low-dose-rate extrapolations of animal carcinogenicity data was evaluated mathematically. Based on analyses of data from animal experiments and data generated by computer simulation, the upper confidence limit on the added risk is approx linear at low dose rates, even when the dose response trend is nonlinear. When test data show a definite linear trend, both upper and lower confidence limits on the added risk should be approx linear, and they should differ by no more than a factor of about 10 for experiments involving several dozen tumor-bearing animals. When the trend does not have a definite linear component, the upper and lower confidence limits on added risk can be expected to differ much more widely; only the upper confidence limits will be stable and meaningful. These conclusions should be applicable to continuous exposure to any direct-acting carcinogen. (29 refs.)

77-5011 **The Effect of Water-Soluble Chemicals on the Growth and Mitosis of Primary Newborn Rat Kidney Cells in Culture.** (Eng.) Hooson, J. (Pathology Dept., British Industrial Biological Res. Assoc., Woodmansterne Rd., Carshalton, Surrey, England); Grasso, P. *Toxicology* 7(1): 1-10; 1977.

The growth rate and mitotic activity were measured in primary cultures of rat kidney cells following 15-30 min exposure to aqueous solutions of various known and suspected carcinogens and noncarcinogenic chemicals. All the proximate carcinogens and two suspected carcinogens depressed cellular growth rate and division, whereas noncarcinogens and precarcinogens tested did not have this effect. It is suggested that growth and mitotic inhibition could be used as a marker in screening procedures for chemical carcinogens. (38 refs.)

77-5012 **Effects of Chemical Carcinogens on Fetal and Placental Development in the Rat (Meeting Abstract).** (Eng.) Tanaka, T. (Aichi Cancer Center, Nagoya, Aichi, Japan). *Teratology* 16(1): 86; 1977. (no refs.)

77-5013 **The Effects of Chemical Carcinogens on Newborn Epidermal Cells in Culture (Meeting Abstract).** (Eng) Miller, D. R. (Biology Division, Oak Ridge Natl. Lab., Oak Ridge, TN 37830); Viaje, A.; Bracken, W. M.; Slaga, T. J. *In Vitro* 13(3): 192; 1977. (no refs.)

77-5014 **Age-related and Carcinogen-induced Changes of the Extracellular Growth Factor Requirements for Cell Proliferation In Vitro (Meeting Abstract).** (Eng.) Swierenga, S. H. (National Research Council of Canada, Ottawa, Canada, K2A0R6); Whitfield, J. F. *In Vitro* 13(3): 164; 1977. (no refs.)

77-5015 **In Vitro Transformation of Diploid Human Cells with Chemical Carcinogens (Meeting Abstract).** (Eng) Milo, G. E. (Dept. Physiology Chemistry and Veterinary Pathobiology, Ohio State Univ., Columbus, OH 43210); DiPaolo, J. A. *In Vitro* 13(3): 193; 1977. (no refs.)

77-5016 **In Vitro Testing for Chemical Carcinogens: Transformation Assays in Mammalian Cells (Meeting Abstract).** (Eng) Casto, B. C. (BioLabs., Inc., Northbrook, IL 60062). *In Vitro* 13(3): 191-192; 1977. (no refs.)

77-5017 **Behavior of Chemically Treated and Nontreated Hamster Cells During Long Term Subculture In Vitro (Meeting Abstract).** (Eng) Papadopoulo, D. (Fondation Curie-Institut du Radium, 26 rue d'Ulm, 75005 Paris); Levy, S.; Chamaillard, L.; Hubert-Habart, M.; Sabharwal, P. S.; Markovits, P. *In Vitro* 13(3): 186; 1977. (no refs.)

77-5018 **Control of Clonal Growth of an Epithelial Liver Cell Line (Meeting Abstract).** (Eng) Starkey, J. R. (Washington State Univ., Pullman, WA 99164); Talmadge, J. T.; Hosick, H. L. *In Vitro* 13(3): 179; 1977. (no refs.)

77-5019 **Sensitivity of Early vs Late Passages of a Rat Hepatocyte Culture for Toxicological Studies of**

Carcinogens (Meeting Abstract). (Eng) Schaeffer, W. I. (Univ. Vermont, Burlington, VT 05401); Heintz, N. H.; Chuang, A. H.; Bresnick, E. *In Vitro* 13(3): 154; 1977. (no refs.)

77-5020 **The Interrelation of Guanosine 3′, 5′ Cyclic Monophosphate (cGMP) and Adenosine 3′,5′ Cyclic Monophosphate (cAMP) in Isolated Hepatocytes when Exposed to Chemical Carcinogens (Meeting Abstract).** (Eng.) Lappe, R. (Dept. Pharmacology, Indiana Univ. Sch. Medicine, Indianapolis, IN 46202); Wagle, S. R. *Pharmacologist* 19(2): 204; 1977. (no refs.)

See also:
* (Rev.): 77-4801, 77-4802, 77-4803, 77-4804, 77-4805, 77-4806, 77-4807, 77-4808, 77-4809, 77-4810, 77-4811, 77-4812, 77-4813, 77-4814, 77-4815, 77-4816, 77-4817, 77-4818, 77-4819, 77-4820, 77-4821, 77-4822, 77-4823, 77-4824, 77-4825, 77-4827, 77-4828, 77-4829, 77-4832, 77-4837, 77-4838, 77-4865, 77-4866, 77-4868, 77-4869, 77-4871.
* (Phys.): 77-5038, 77-5047, 77-5048, 77-5050, 77-5053.
* (Viral): 77-5095, 77-5098, 77-5108.
* (Immun.): 77-5178, 77-5179, 77-5180, 77-5182, 77-5184, 77-5188, 77-5198, 77-5215, 77-5218, 77-5220, 77-5221, 77-5232.
* (Path.): 77-5245, 77-5262, 77-5263, 77-5275, 77-5276, 77-5281, 77-5300, 77-5307, 77-5319.
* (Epid.-Biom.): 77-5327, 77-5328, 77-5329, 77-5330, 77-5331, 77-5332, 77-5334. 77-5344, 77-5346, 77-5350, 77-5351.

77-5021 **Mesenteric Hemopoietic Colonies: Occurrence in BALB/c Mice after Transplantation of Syngeneic Normal or Leukemic Hemopoietic Cells.** (Eng) Umar, M. H. (Dept. Experimental Pathology, Medical Faculty, Erasmus Univ., P.O. Box 1738, Rotterdam, Netherlands); van Griensven, L. J. *Exp Hematol* 5(4): 281-290; 1977.

The histologic features of mesenteric hemopoietic colonies (MHC) formed in BALB/c mice during recovery from radiation damage are described. Cellular foci were present in the mesentery of all unirradiated BALB/c recipients 7 days after injection of syngeneic bone marrow or spleen cells. The MHC were composed of cells histologically comparable to those injected. In mesenteries from lethally irradiated mice, similar foci of proliferating cells were observed. The number and size of the MHC increased with time, becoming confluent as early as 10 days after cell injection. Bone marrow and spleen cells from mice infected with Rauscher leukemia virus also produced MHC and spleen colonies after ip injection into lethally irradiated mice. The MHC were generally of the mixed cell type. In addition to the undifferentiated cells in the MHC, cells with limited differentiation and/or retarded maturation were identified. A survival period of 80 days after lethal irradiation and ip transplantation of normal bone marrow or spleen cells was obtained. Bone marrow and spleen were almost completely repopulated at 80 days. These data indicate that under certain conditions, the mesentery of BALB/c mice can act as a field of ectopic hemopoiesis. All mice receiving normal or neoplastic bone marrow or spleen cell suspensions developed mesenteric hemopoietic foci; lethal irradiation of mice before transplantation made this effect even more pronounced. (27 refs.)

77-5022 **The Effect of Immunotherapy with BCG on the Development of Radiostrontium (^{90}Sr)-induced Osteosarcoma. A Roentgenographical, Light Microscopical and Ultrastructural Study in Mice.** (Eng) Larsson, S. E. (Dept. Orthopedic Surgery, Univ. Umea, Umea, Sweden); Lorentzon, R.; Boquist, L. *Acta Pathol Microbiol Scand [A]* 85(4): 433-446; 1977.

The effect of BCG therapy on radiostrontium-induced sarcomas in CBA mice was investigated. ^{90}Sr was administered by a single ip injection of $^{90}Sr(NO_3)_2$ with a specific activity of 100 mCi/ml. The dosage was 0.7 mCi/g body wt. Between 70 and 135 days after the radiostrontium injection, each animal was inoculated sc with 1.0 mg BCG in 0.2 ml Sauton solution; the inoculation was repeated three more times at 3 wk intervals for a total of four doses. During the observation period of 420 days, 89.5% of the BCG-treated and 90.5% of the BCG-untreated (control) animals developed osteosarcomas. In spite of a slight tendency toward earlier tumor incidence in the BCG-treated animals, the differences between the groups for time of tumor appearance or tumor incidence were not significant. Most of the lesions were in the spinal column and femur (32.5% and 27.9%, respectively), with the tibia, humerus, and pelvis making up the balance. The distribution was not statistically significant between the groups, nor was mortality. Tumors in BCG-treated animals showed a slower growth rate, probably due to an immunological effect. The histology of the tumors is described. (16 refs.)

77-5023 **The Ultrastructure of Skeletal Haemangiosarcomas Induced in Mice by Strontium-90.** (Eng) Ash, P. (MRC Radiobiology Unit, Harwell, Didcot, Oxon, England); Loutit, J. F. *J Pathol* 122(4): 209-218; 1977.

Samples of nonosteogenic tumors induced by strontium-90 in male CBA and C3H mice, which were diagnosed as hemangiosarcomas, were examined electron microscopically, and their ultrastructure was compared with that of fibroblastic osteosarcomas. The major feature was abundant vasoformation, with the vascular channels varying in shape and size and in the character of their lining cells. Some vascular channels were lined by cuboidal cells that were crowded together and surrounded by a basement membrane. Others were lined by an attenuated endothelium, and they often formed networks. The tumor cells showed great variation in shape, size, and ultrastructure and were sometimes enclosed by a basement membrane. It is concluded that the ultrastructure of these tumors supports the diagnosis of hemangiosarcoma, rather than fibroblastic osteosarcoma. Unlike normal vascular endothelium, the tumor endothelium does not contain alkaline phosphatase. Either the tumors are derived from primitive stromal progenitors and mimic vascular endothelium, or the endothelial precursor cells, of which these may be malignant variants, do not develop their alkaline phosphatase until they are nearly mature. The presence of a basement membrane and microfilaments supports the view that the tumor cells may originate from vascular endothelial cells or their precursors. (20 refs.)

77-5024 **Histologic Types of Bronchogenic Cancer in Relation to Different Conditions of Radiation Exposure.** (Eng) Horacek, J. (District Inst. National Health, OUNZ, Dept. Pathology, Karlovy Vary, Czechoslovakia); Placek, V.; Sevc, J. *Cancer* 40(2): 832-835; 1977.

The risk of lung cancer among uranium miners was evaluated, and the various histologic types were compared in relation to various conditions of radiation exposure. The study comprised 115 miners with lung cancer and 326 men with lung cancer who were not uranium miners (matched controls). There was a 12% higher fraction of small cell undifferentiated cancer (due to the increase in oat cell carcinoma) and a lower fraction of adenocarcinoma than among the miners than among the controls. For the miner group, which was followed for 21-26 yr from the start of exposure, both the small cell and epidermoid types were elevated over expected values. The frequency of these two major histologic types may be influenced by the level of cumulated radiation exposure and by the time course of cumulation of exposure in a different way. Lower total cumulated exposure or lower initial exposure was probably responsible for the increase of the small cell cancer only, and the considerable rise of epidermoid cancer appeared after higher total cumulated exposure or after a high initial exposure. (9 refs.)

77-5025 **Polonium-210 in Bombay Diet.** (Eng) Khandekar, R. N. (Air Monitoring Section, Bhabha Atomic Res. Centre, Trombay, Bombay-400085, India). *Health Phys* 33(2): 148-150; 1977.

Polonium-210 levels were determined in most of the foods in a typical Bombay diet and the total daily intake of ^{210}Po by an individual living in the city of Bombay was estimated. ^{210}Po was measured in 7 categories of food: cereals, legumes, vegetables, milk and milk products, meat, fish, and fruits. From data on the consumption of the various foods and the mean concentration of ^{210}Po in the food samples, the concentration of ^{210}Po in Bombay diet was found to be 1.4 pCi/day. The amount reaching the blood from various sources was estimated using International Commission on Radiological Protection values for the fraction of ^{210}Po absorbed. It is estimated that ^{210}Po in the diet accounts for 75% (0.084 pCi) of the total ^{210}Po reaching the blood every day. Daily intake of ^{210}Po through the air accounts for 17% of ^{210}Po in the blood, drinking water for 8%. (12 refs.)

77-5026 **^{239}Pu Contamination in Snakes Inhabiting the Rocky Flats Plant Site.** (Eng) Geiger, R. A. (Savannah River Ecology Lab., Drawer E, Aiken, SC 29801); Winsor, T. F. *Health Phys* 33(2): 145-148; 1977.

A study was conducted to determine whether tissues from snakes inhabiting the Rocky Flats plant site immediately downwind from an area previously used to store barrels of plutonium-laden cutting oil contained detectable amounts of ^{239}Pu. Pu assay of the lung, liver, and bone from nine snakes consisted of ashing, total dissolution, electrodeposition, and α-spectrometry. In 20/27 tissues sampled, the activity was $\leq$ 0.1 disintegration/min (dpm)/g, and in no case did the concentration exceed 1.0 dpm/g. There was no detectable activity in 8/9 lung samples. Activities in the liver samples ranged from 0.01 to 0.44 dpm/g and skeletal sample activities ranged from nondetectable to 0.56 dpm/g. Low ^{239}Pu concentrations in the tissues and the lack of any significant correlation between distance from the presumed source of contamination and ^{239}Pu concentrations in the liver or bone may be partly due to the transiency of certain species of snakes. Although the interpretation of the tissue concentrations is complicated, preliminary data suggest that snakes are not an important organism in the redistribution of ^{239}Pu. (17 refs.)

77-5027 **Radiation-associated Hyperparathyroidism: A New Syndrome?** (Eng) Prinz, R. A. (Veterans Admin. Hosp., Hines, IL 60141); Paloyan, E.; Lawrence, A. M.; Pickleman, J. R.; Braithwaite, S.; Brooks, M. H. *Surgery* 82(3): 296-302; 1977.

A retrospective and prospective study was conducted to determine whether there is a relationship between radiation exposure and the development of parathyroid hyperactivity. Of 89 patients who underwent surgery for primary hyperparathyroidism in the last 12 yr, 27 (13 men, 14 women, 24-69 yr old) had a history of radiation therapy to the head and neck for benign disease. The age at which radiation therapy was administered ranged from 5 mo to 30 yr. The interval between radiation exposure and parathyroidectomy was 10-47 yr. Accurate information on radiation dose was known in six patients, and it ranged from 300 to 750 rads. Fourteen patients had hyperplasia or multiglandular diseases, and 13 had single adenomas. Thyroid carcinoma was associated with hyperparathyroidism in four patients (2 follicular carcinomas, 1 sclerosing carcinoma, and 1 mixed papillary-follicular carcinoma), and six had benign thyroid tumors. There was no discernible thryoid abnormality in the other 17 patients. These findings suggest that radiation may be a significant factor for explaining what appears to be an increase in the incidence of primary hyperparathyroidism. (22 refs.)

77-5028 **Hyperparathyroidism in Persons Treated with X-Rays for Tuberculous Cervical Adenitis.** (Eng) Tisell, L. E. (Dept. Surgery II, Univ. Goteborg, Goteborg, Sweden); Hansson, G.; Lindberg, S.; Ragnhult, I. *Cancer* 40(2): 846-854; 1977.

Follow-up examinations were performed on 100 persons who had been treated with x-rays for tuberculous adenitis between 1930 and 1946 to determine if there is an increased incidence of hyperparathyroidism (HPT) after radiation exposure. Neck exploration was carried out on six patients with verified hypercalcemia and signs and symptoms compatible with HPT. Four other individuals had hypercalcemia but were asymptomatic. Six individuals with thyroid masses were also operated upon when examination of fine-needle specimens gave suspicions of malignancy. Biopsies were taken from normal-appearing parathyroid glands in most cases and from the thryoid gland in all. All of the six hypercalcemic patients with HPT symptoms had pathological parathyroid glands. Examiation of the six individuals with thryoid masses revealed the resence of papillary carcinoma in three, an oxyphil adenoma n one, and a follicular adenoma in one; three of these five atients also had pathological parathyroid glands. The mean bsorbed dose in the parathyroid glands varied between 75 nd 2,200 rads; HPT did not occur with < 300 rads. HPT eveloped in 3/39 cases after doses of 300-600 rads, in 4/28 ases after doses of 600-1,200 rads, and in 4/6 cases after oses > 1,200 rads. All the patients operated on are now ormocalcemic. These findings indicate that HPT is a more ommon late complication of neck radiotherapy than thyroid arcinoma. (27 refs.)

77-5029 **Thyroid Cancer Following Scalp Irradiation.** (Eng.) Modan, B. (Dept. Clinical Epidemiology, Chaim Sheba Medical Center, Tel Hashomer, Israel); Ron, E.; Werner, A. *Radiology* 123(3): 741-744; 1977.

A follow-up study of 10,902 persons irradiated for pediatric scalp tinea shows a sixfold increase in the risk of thyroid cancer as compared with two matched control groups. The original mean dose given to the thyroid was < 9 rads. The carcinogenic risk of low-level radiation is discussed. (19 refs.)

77-5030 **Salivary Gland Neoplasms as a Late Consequence of Head and Neck Irradiation.** (Eng) Schneider, A. B. (Dept. Medicine, Michael Reese Hosp. and Medical Center, 29th St. and Ellis Ave., Chicago, IL 60616); Favus, M. J.; Stachura, M. E.; Arnold, M. J.; Frohman, L. A. *Ann Intern Med* 87(2): 160-164; 1977.

The presence of salivary gland tumors was investigated in 1,922 patients (1,273 interviewed and examined physically and 649 reached by questionnaire) who had received radiation to the tonsil-nasopharyngeal area between 1939 and 1962. Twenty-seven tumors (19 benign and 8 malignant) were found in this group compared with an expected 0.2 malignant and < 1 benign tumor. The latent period between initial radiation treatment and diagnosis was 7-32 yr. After the first 15 yr, the incidence (77 cases/10^5 subjects/yr) has remained constant and shows no indication of declining. No difference was seen between patients with benign and malignant tumors with respect to latency, age at initial treatment, age at diagnosis, dose, or sex. The constant incidence rate for salivary gland tumors, even after 35 yr, emphasizes the importance of continued observation for patients who received childhood irradiation. (20 refs.)

77-5031 **Radiation Induced Carcinoma of the Temporal Bone.** (Eng) Ruben, R. J. (Dept. Otorhinolaryngology, Albert Einsten Coll. Medicine, Yeshiva, Univ., 1300 Morris Park Ave., Bronx, NY 10461); Thaler, S. U.; Holzer, N. *Laryngoscope* 87(10/part 1): 1613-1621; 1977.

The case of a 29-yr-old man who developed temporal bone carcinoma of the head as a result of radiation therapy is presented. The patient had undergone craniotomies at age 5, 7, and 17 for recurrent cerebellar astrocytoma; he had subsequently received 14,000 rads to the head by kilo and supra voltage. The portals included both temporal bones. Twelve years after his last radiation treatment, he underwent a right radical mastoidectomy for removal of an extensive cholesteatoma of the middle ear and mastoid. Six mo later, a left cholesteatoma was removed by left radical mastoidectomy. Histologic examination of the specimen revealed transformation into well differentiated squamous cell carcinoma; 2 mo later, a left temporal bone resection was performed. He was free of recurrent disease 1 yr later. (19 refs.)

77-5032 **Radiation-induced Extraskeletal Fibrosarcoma. Simulating Locally Recurrent Carcinoma of Breast.** (Eng) Friedman, I. H. (1175 Park Ave., New York, NY 10028); Mori, K.; Kabakow, B. *NY State J Med* 77(12): 1932-1935; 1977.

A 66-yr-old woman presented with radiation-induced extraskeletal fibrosarcoma 7 yr after radical mastectomy and 4,000 rads total tumor dose for invasive, scirrhous carcinoma of the breast. She had also undergone resection for adenocarcinoma of the sigmoid colon. The fibrosarcoma was located in the mastectomy scar and recurred several times. Reasons for attributing the lesion to the radiation treatment are discussed. (19 refs.)

77-5033 **Breast Neoplasms in Women Treated with X-Rays for Acute Postpartum Mastitis.** (Eng) Shore, R. E. (Inst. Envirnomental Medicine, New York Univ. Medical Center, 550 First Ave., New York, NY 10016); Hempelmann, L. H.; Kowaluk, E.; Mansur, P. S.; Pasternack, B. S.; Albert, R. E.; Haughie, G. E. *J Natl Cancer Inst* 59(3): 813-822; 1977.

A study was made of the incidence of breast cancer in 571/606 women given x-ray therapy for acute postpartum mastitis over a 34-yr period. The results were compared to those for three nonirradiated control groups: sisters of the treated women, unirradiated women with acute postpartum mastitis, and sisters of the unirradiated mastitis patients. The irradiated patients received a mean dose of 246 rads of both breasts and had an overall relative risk of breast cancer of 2.2 for postirradiation years 10-34 and 3.6 for years 20-34. The dose-response curve for malignant and benign tumors was compatible with a linear model, and for comparable total doses, carcinogenicity was not reduced by dose fractionation. Women $\geqslant$ 30 yr of age at the time of treatment had as great a risk of excess breast cancer as did younger women. The overall absolute risk of excess breast cancer was about 8-10 cases/10^6 women/rad/year, an increase of about 0.5%/rad. (38 refs.)

77-5034 **Breast Cancer in Women after Repeated Fluoroscopic Examinations of the Chest.** (Eng) Boice, J. D. (Epidemiologic Studies Branch, Bureau Radiological Health, U.S. Dept. Heath, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857); Monson, R. R. *J Natl Cancer Inst* 59(3): 823-832; 1977.

A follow-up study was conducted on 1,764 women who had been discharged between 1930 and 1954 from two tuberculosis sanatoria in Massachusetts. Of these, 1,047 had been examined fluoroscopically an av of 102 times over a period of several years (FE group) and 717 had not be subjected to fluoroscopy (controls). Excess breast cancer became apparent among the FE group 15 yr after the initial exposure and still continues after 40 yr of observation. A total of 17.7 excess cases of breast cancer (41 observed vs 23.3 expected) has been reported among the FE patients for whom data were available, whereas there was no excess (15 vs 14.1) in the controls. The greatest absolute risk of excess breast cancer (13.3 cases/10^6 women-years/fluoroscopy) was noted in women who were first treated between 15 and 19 yr of age. No excess incidence of cancer was seen in patients $\geq$ 30 yr of age at the time of first exposure. The risk of excess breast cancer increased with increasing radiation dose, and the data were consistent with a linear dose-response relationship. The overall absolute risk of excess breast cancer in women living $\geq$ 10 yr beyond the first exposure was 6.2 cases/10^6 women-years/rad. (31 refs.)

77-5035 **Inactivation and Mutation of Cultured Mammalian Cells by Aluminium Characteristic Ultrasoft X-Rays. III. Implications for Theory of Dual Radiation Action.** (Eng) Goodhead, D. T. (Medical Res. Council Radiobiology Unit, Harwell, Didcot, Oxon OX11 ORD, England). *Int J Radiat Biol* 32(1): 43-70; 1977.

Microdosimetric distributions were calculated for aluminum K characteristic ultrasoft x-rays and ^{4}He ion tract intersections and applied to biological results obtained with these irradiations on various systems. Studies with V79 Chinese hamster cells and HF19 human fibroblasts revealed that a simple analysis in terms of site diameter is inadequate. The relative biological effectiveness values observed cannot be brought in line with calculated values unless a variable is introduced. However, this variable produces mathematical inconsistencies in the model. The use of a distance model interpretation instead of a theory of dual radiation action or a site model interpretation may help explain some of the discrepancies, but the form of the required function is not yet known. (30 refs.)

77-5036 **DNA Repair in Human Lymphocytes.** (Eng.) Agarwal, S. S. (Inst. Cancer Res., Fox Chase Cancer Center, Philadelphia, PA 19111); Brown, D. Q.; Katz, E. J.; Loeb, L. A. *In: Genetics of Human Cancer.* Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F. (New York: Raven Press): Progress in Cancer Research and Therapy 3: 365-368; 1977.

The amount of DNA polymerase activity and $[^3H]$-thymidine uptake in x-irradiated lymphocytes was determined following stimulation with phytohemagglutinin. Results show that this test system can be used to screen for defects in DNA repair. (8 refs.)

77-5037 **Effect of Radiation and Contrast Media on Chromosomes. Preliminary Report.** (Eng) Adams, F. H. (Div. Cardiology, Dept. Pediatrics, UCLA Sch. Medicine, Los Angeles, CA 90024); Norman, A.; Mello, R. S.; Bass, D. *Radiology* 124(3): 823-826; 1977.

The effect of in vivo angiocardiography and in vitro Renografin 76 (a 76% solution of methylglucimine diatrizoate and sodium diatrizoate) and 125 kilovolt (kV) x-rays on chromosome aberrations or micronuclei in lymphocytes from seven patients was investigated. In vivo fluoroscopy was performed with 64- to 65-kV peak x-rays. An absorbed dose rate of 4 rads/hr was estimated from the entrance and exit doses. Chromosome damage produced during angiocardiography corresponded to an av absorbed dose of 50 rads, an order of magnitude higher than that estimated from exposure rates. In vitro studies indicated that the damage was due to an increased absorption of x-rays compared to blood and the breakage of chromosomes even in the absence of x-rays. Whether this increased exposure because of contrast media (damage in absence of x-rays) is due to the major constituents of the agents or minor constitutents produced during manufacture, storage, or use is unknown. (9 refs.)

77-5038 **Induction of Hepatic Aryl Hydrocarbon Hydroxylase in C57BL Mice by Ionizing Radiation.** (Eng) Prasad, N. (Dept. Radiology, Baylor Coll. Medicine, Houston, TX 77030); Prasad, R.; Thornby, J.; Bushong, S. C.; North, L. B.; Harrell, J. E. *Cancer Res* 37(10): 3771-3773; 1977.

Inbred C57BL mice were exposed to 100, 500, or 1,000 rads of whole-body x-irradiation. Another group of mice received injections of 3-methylcholanthrene (100 mg/kg) in corn oil, and a control group had no treatment. Forty-eight hours after treatment, the animals were killed and hepatic aryl hydrocarbon hydroxylase (AHH) activity was measured spectrophotofluorometrically. Each treated group had a significantly increased induction of AHH compared with the control group. Although radiation appeared to have a dose-related effect on AHH induction, the increase with dose level was not statistically significant. (26 refs.)

77-5039 **Differences in Strand Break Repair Between Fibroblasts from Different Species (Meeting Abstract).** (Eng) Macieira-Coelho, A. (Institut de Cancerologie et Immunogenetique (INSERM-U50), 94800, Villejuif, France); Diatloff, C.; Loria, E. *In Vitro* 13(3): 186; 1977. (no refs.)

77-5040 **Dicentric Yields Induced by γ-Radiation and Chromosome Arm Number in Primates.** (Eng.) Hirai, M. (Div. Genetics, Natl. Inst. Radiobiological Sciences, Anagawa, Chiba 280, Japan); Nakai, S. *Mutat Res* 43(1): 147-157; 1977.

The effect of chromosome arm number on the yield of dicentric chromosomes was evaluated by examining the frequencies of γ-ray-induced chromosome aberrations using peripheral lymphocytes from three different primate species: the squirrel monkey *Saimiri sciureus* (arm number 77), the crab-eating monkey *Macaca fascicularis* (arm number 83), and the slow loris *Nycticebus coucang* (arm number 99). Three healthy males from each species were studied. Irradiated blood samples were cultured by the same technique as that commonly used for human lymphocytes. The yields of dicentrics and dicentrics plus rings at doses of 100, 200, and 300 rads of γ-irradiation were not significantly different among the three species, in spite of the differences in chromosome arm number. Dose-response relationships for these species were consistent with that for man. Statistical analysis indicated that the expected dicentric yields caclulated from the arm number model were significantly different from the observed yields at 200 and 300 rads. It is concluded that there is no correlation between the dicentric yield and effective chromosome arm number and that the chromosomal radiosensitivity of the three primate species is essentially the same as that of man, at least in the lymphocyte system. (33 refs.)

77-5041 **Excision of Gamma-ray-induced Thymine Lesions by Preparations from Ataxia Telangiectasia Fibroblasts.** (Eng.) Remsen, J. F. (Dept. Biochemistry, J. Hillis Miller Health Center, Univ. Florida, Gainesville, FL 32610); Cerutti, P. A. *Mutat Res* 43(1): 139-145; 1977.

Four Ataxia telangiectasia skin fibroblast strains (AT CRL 1312, AT CRL 1343, AT GM 367, and AT 4BI) were capable of excising aerobic gamma-ray products of the 5,6-dihydroxydihydrothymine type from exogenous DNA substrates. (19 refs.)

77-5042 **The Effect of Cobalt-60 Irradiated Fetal Bovine Serum in Cell Culture (Meeting Abstract).** (Eng) Matchett, A. (Veterinary Services Lab., Ames, IA 50010); Wessman, S. J.; Andrew, B. B.; Mason, P. S. *In Vitro* 13(3): 153; 1977. (no refs.)

77-5043 **Spontaneous, Ultraviolet and Ionizing Radiation Mutagenesis in Two Auxotrophic Strains of *Salmonella typhimurium* Carrying an R Plasmid.** (Eng) MacPhee, D. G. (Genetics Dept. La Trobe Univ., Bundoora, Victoria 3083, Australia). *Mutat Res* 45(1): 1-6; 1977.

Experiments were performed to determine whether the R-Utrecht factor increases the susceptibility of *Salmonella typhimurium* to spontaneous mutation and to ionizing radiation (α) as it does with UV radiation. Derivatives of strain LT2 were used. The R-Utrecht plasmid significantly increased spontaneous and γ-induced mutation yields in one of the strains. However, in the other strain, increased susceptibility to UV effects did not appear to be correlated with spontaneous or γ-induced mutations, which were only slightly increased. (8 refs.)

77-5044 **Repair of Pyrimidine Dimers in Radiation-sensitive Mutants *rad3, rad4, rad6,* and *rad9* of *Saccharomyces cerevisiae*.** (Eng) Prakash, L. (Dept. Radiation Biology and Biophysics, Univ. Rochester Sch. Medicine and Dentistry, Rochester, NY 14642). *Mutat Res* 45(1): 13-20; 1977.

The fate of UV-induced dimers in *rad3, rad4, rad6* and *rad9* mutants of *Saccharomyces cerevisiae* were studied using the ability of T4 UV endonuclease and extracts of *Micrococcus luteus* to produce single-strand breaks in DNA containing pyrimidine dimers. The *rad3* and *rad4* mutants were defective in dimer excision; *rad6* and *rad9* were proficient in dimer repair. (30 refs.)

77-5045 **Normal Endonuclease Activities for Damaged DNA During Hepatocarcinogenesis.** (Eng) Teebor, G. W. (Dept. Pathology, New York Univ. Medical Center, New York, NY 10016); Duker, N. J.; Becker, F. F. *Biochim Biophys Acta* 477(2): 125-131; 1977.

The activities of two endonucleases that attack damaged DNA were assayed in extracts of male ACI rat liver at different states of experimental carcinogenesis. The rats were fed a diet containing N-2-acetylaminofluorene. Double-stranded, covalently closed DNA from phage PM2 was damaged by UV radiation by heating at acid pH and used as a substrate for endonucleases specific for UV DNA damage and for

DNA apurinic sites, respectively. Endonuclease activities were assayed by measuring the conversion of superhelical DNA to the nicked form by velocity sedimentation in neutral CsCl. The enzyme activities were also assayed in untreated rats. At none of the phases of the hepatocarcinogenic regimen was either endonuclease activity depressed. It is concluded that suppression of excision repair probably does not take place during experimental carcinogenesis. (24 refs.)

77-5046 **Postreplication Repair in Xeroderma Pigmentosum Fibroblast Cells (Meeting Abstract).** (Eng) Minka, D. F. (West Virginia Univ., Morgantown, WV 26506); Nath, J. *In Vitro* 13(3): 201; 1977. (no refs.)

77-5047 **Sister Chromatid Exchanges in Human Lymphocytes Exposed to 8-Methoxypsoralen and Long Wave UV Radiation Prior to Incorporation of Bromodeoxyuridine.** (Eng) Mourelatos, D. (Cytogenetics Lab., Dept. Pathology, Ninewells Medical Sch., Univ. Dundee, Dundee, DD2 1UB, Scotland); Faed, M. J.; Johnson, B. E. *Experientia* 33(8): 1091-1093; 1977.

The effect of 8-methoxypsoralen (8-MOP) and long wave UV radiation (319 to 390 nanometers) on the production of sister chromatid exchanges (SCE) in human lymphocytes from healthy adults was investigated using bromodeoxyuridine (BrdU) technique. The addition of 40 μM 8-MOP had no appreciable effect on the rate of SCE; but when the cells were irradiated 15 to 30 min after 8-MOP addition, there was an increase in the mean SCE rate. This increase in SCE occurred only in some of the cells. The proportion of cells with SCE above 18 (control number) was 10% at 0.002 μM 8-MOP, 21% at 0.2 μM, 36% at 2 μM and 57% at 20 μM. In the presence of 20 μM 8-MOP, increased SCE rates were obtained with increasing exposure time up to about 15 min; after this, there is no further increase other than that due to UV alone. This same time effect held for other doses of 8-MOP. It is concluded that damage resulted when UV exposure occurred in G_0, when the chromosomes had not incorporated BrdU into either strand; this UV-activated 8-MOP damage is dose-dependent and some of it may not be repaired until post-replication. (14 refs.)

77-5048 **DNA Crosslinking in Cells Exposed to Psoralens and UV Light (Meeting Abstract).** (Eng) Peterson, S. P. (Univ. California, Irvine, Irvine, CA 92717); Hearst, J. E.; Berns, M. W. *In Vitro* 13(3): 153-154; 1977. (no refs.)

77-5049 **Mutagenesis by Fluorescent Light in Mammalian Cell Cultures.** (Eng.) Jostes, R. F. (Dept. Radiology and Radiation Biology, Colorado State Univ., Fort Collins, CO 80523); Dewey, W. C.; Hopwood, L. E. *Mutat Res* 42(1): 139-144; 1977.

Chinese hamster ovary cells exposed to fluorescent light during the first 16-17 hr of the cell cycle (G1, S, and G2) always had a higher mutant frequency than those kept in the dark. In addition, an apparent dose response was noted. (20 refs.)

77-5050 **Effect of Fluorescent Light and Oxygen on Chromosomes, Cytology, and Neoplastic Transformation of Mouse Cells in Culture (Meeting Abstract).** (Eng) Sanford, K. K. (Lab. Biochemistry, NCI, Bethesda, MD 20014); Parshad, R.; Handleman, S. L.; Jones, G. M.; Price, F. M. *In Vitro* 13(3): 181; 1977. (no refs.)

77-5051 **Mammary Neoplasia in the Rat Following High-Energy Neutron Irradiation.** (Eng.) Montour, J. L. (Medical Coll. Virginia, Box No. 31, 1200 E. Broad St., Richmond, VA 23298); Hard, R. C.; Flora, R. E. *Cancer Res* 37(8, part 1): 2619-2623; 1977.

Young female Sprague-Dawley rats were exposed to single doses of 35-MeV (max-energy) neutrons, and dose-response relationships were examined 11 mo later. During the 11 mo, 2/31 nonirradiated rats developed a single fibroadenoma and 39/135 irradiated rats developed 42 breast tumors. Tumors originating from sites other than the breast included lymphocytic-type lymphosarcoma, osteogenic sarcoma, myxosarcoma, fibrosaroma, and angiosarcoma. Analysis of the relationship between the number of breast tumors per rat and radiation dose indicated that the number of tumors per rat is dependent upon (dose) to the power *n*, where *n* is slightly less than unity. When the data were modified to account for the number of breasts at risk, the dose response approached a straight line. These findings are consistent with a model of carcinogenesis in which a single high-LET (linear energy transfer) particle traversing a single cell can cause a carcinogenic alteration. The relative biological effectiveness of the 35-MeV neutrons compared to γ-rays for breast tumor induction was 4.3, based on the slopes of the linear responses to both types of radiation. With the best-fit curves for both neutrons and γ-rays, the relative biological effectiveness increased from 5.0 at 40 rads of neutrons to 13.8 at 2.5 rads of neutrons. (11 refs.)

77-5052 **Changes in Pulmonary Surfactant and Phosphatidylcholine Metabolism in Rats Exposed to**

Chrysotile Asbestos Dust. (Eng) Tetley, T. D. (Dept. Biochemistry, Univ. Coll., Post Office Box 78, Cardiff CF11 XL, Wales); Richards, R. J.; Harwood, J. L. *Biochem J* 166(3): 323-329; 1977.

Pulmonary surfactant was isolated from male Wistar rats that had been exposed to chrysotile asbestos dust for 3 days to 15 wk. The asbestos- treated rats showed a progressive increase in the amount of surfactant; after 15 wk the pulmonary surfactant content was four times greater in the treated rats than in the untreated controls. No significant change occurred in the total protein or total fatty acid composition of surfactant with exposure. The increase in surfactant phosphatidylcholine normally seen on maturation of the rat lung was accelerated by asbestos exposure. Phosphorylcholine glyceride transferase activity increased in lung homogenates and free cell populations. Lysosomal phospholipase A was relatively unaffected by dust exposure. It is suggested that the increase in surfactant could be due to an increase in its synthesis without a corresponding alteration in its degradation. (72 refs.)

77-5053 **Relationship Between Occupations and Asbestos-Fibre Content of the Lungs in Patients with Pleural Mesothelioma, Lung Cancer, and Other Diseases.** (Eng) Whitwell, F. (Dept. Pathology, Broadgreen Hosp., Thomas Drive, Liverpool L14 3LB, England); Scott, J.; Grimshaw, M. *Thorax* 32(4): 377-386; 1977.

The asbestos fiber contents of the lungs from 100 pleural mesothelioma patients, 100 control patients (who had died from conditions other than lung cancer or industrial lung disease), and 100 lung cancer patients without industrial lung disease were analyzed to determine which pleural mesotheliomas were asbestos-induced and which were spontaneous. In the mesothelioma group, 88/100 patients had a history of asbestos exposure; 87/88 showed > 20,000 fibers/g of dried lung tissue, and 73/88 had > 100,000 fibers/g lung tissue. The number of asbestos fibers corresponded roughly to the degree of asbestosis. It is suggested that there is a definite dose relationship between the number of asbestos fibers in the patients' lungs and the presence of asbestos-induced mesotheliomas. In both the control and the lung cancer series, 57% of the patients had < 10,000 fibers/g dried lung. This amount is probably harmless and may represent a background urban level created by the widespread use of asbestos in the last half century. The high levels of asbestos found in this study correlated with occupation but not with home environment. (20 refs.)

77-5054 **Serial Pulmonary Function Tests in Patients with Asbestosis.** (Eng.) Britton, M. G. (Pulmonary Res. Unit, Dept. Chest Medicine, London Hosp., London E1, England); Huges, D. T.; Wever, A. M. *Thorax* 32(1): 45-52; 1977.

Serial lung function tests done on 17 patients with asbestosis showed that after a variable interval of time following exposure to asbestos, an initial marked fall in transfer factor preceded any significant decline in vital capacity. There was no significant correlation between lung function test results and the emergence of fatal carcinoma in six cases. (7 refs.)

See also:
* (Rev.): 77-4811, 77-4830, 77-4831, 77-4832, 77-4833, 77-4834, 77-4835, 77-4836, 77-4837, 77-4838, 77-4839, 77-4840.
* (Chem.): 77-4884, 77-4885, 77-4911, 77-5007.
* (Viral): 77-5177, 77-5188, 77-5191.
* (Path.): 77-5258. 77-5260, 77-5274, 77-5307.
* (Epid.-Biom.): 77-5343.

77-5055 **Contact-mediated Suppression of Mitogen-induced Responsiveness by Spleen Cells in Reticuloendotheliosis Virus-induced Tumorigenesis.** (Eng) Carpenter, C. R. (Univ. Texas at Austin, Dept. Microbiology, Austin, TX 78712); Bose, H. R.; Rubin, A. S. *Cell Immunol* 33(2): 392-401; 1977.

Ip inoculation with reticuloendotheliosis virus (REV), a C-type RNA tumor virus, suppressed the response of chicken spleen cells to the mitogens phytohemagglutinin-P (PHA) and lipopolysaccharide (LPS). DNA synthesis (^{3}H-thymidine uptake) was dramatically suppressed, but protein synthesis (^{3}H leucine uptake) and trypan blue dye exclusion were only moderately decreased or unaffected, indicating that viability was not substantially reduced. When mixed at a ratio of 1:1 with spleen cells from birds with reticuloendotheliosis (REs), normal spleen cells (Ns) prestimulated with mitogen were similarly suppressed. Removal of adherent cells did not abrogate the suppressive effects. No suppressor substance was isolated from the supernatant fluids of cultured REs. Moreover, no suppression occurred across 0.4-μm Nuclepore filters in 2-ml double-diffusion chambers. The REV-induced suppression could be transferred to normal cells with the 8,000*g* supernatants and pellets of lysed REs; the reverse transcriptase assay revealed little or no detectable REV in these preparations, indicating that the suppressive agent was not intact REV. Similar preparations from an REV-transformed cell line did not suppress Ns. Centrifugation at 73,500*g* removed suppressing activity from the lysed REs preparations. These results suggest that the suppression in REV-induced tumorigenesis is contact mediated. (46 refs.)

77-5056 **Synthesis of Full-Length DNA Copies of Avian Myeloblastosis Virus RNA in High Yields.** (Eng.) Myers, J. C. (Inst. Cancer Res., Coll. Physicians and Surgeons, Columbia Univ., New York, NY 10032) Spiegelman, S.; Kacian, D. L. *Proc Natl Acad Sci USA* 74(7): 2840-2843; 1977.

Highly purified preparations of AMV reverse transcriptase were used to synthesize high yields of full-length DNA complementary (cDNA) to avian myeloblastosis virus (AMV) RNA. The RNA was prepared from virus obtained from the plasma of infected birds and isolated by sucrose gradient centrifugation in the presence of sodium dodecyl sulfate. AMV RNA was extracted to maximize the proportion of undegraded nucleic acid. Electrophoresis in agarose-methylmercury gels showed that the cDNA had a molecular wt of 2.6×10^6, the same as that of the RNA template. Between 60% and 70% of the DNA synthesized was full-length, equal to the template 35S RNA. Yields were approx 60%-70% of the input RNA. This large cDNA was exclusively single-stranded, and it hybridized completely back to AMV RNA. (20 refs.)

77-5057 **Protein Kinase and Phosphoproteins of Avian Myeloblastosis Virus.** (Eng.) Tsiapalis, C. M. (Meloy Labs., Inc., Springfield, VA 22151) *J Virol* 21(3): 843-848; 1977.

A protein kinase associated with purified virions of avian myeloblastosis virus, BAI strain A, was highly purified by ion-exchange chromatography and gel filtration. Molecular sieving on Sephadex G-200 showed that the enzyme protein had a molecular wt of about 50,000 to 60,000; disk gel electrophoresis in sodium dodecyl sulfate-acrylamide gels revealed the presence of at least two polypeptide chains; and isoelectric focusing on acrylamide gels revealed two protein bands with activity. Of the nonviral proteins used as phosphate acceptors, the greatest phosphorylation rate was obtained with α-casein. Potential physiological substrates for this activity included a specific virion polypeptide of avian myeloblastosis virus. One of the virion polypeptides found in association with reverse transcriptase activity from avian myeloblastosis virus accepted more phosphate than any of nonviral or viral polypeptides examined on the basis of nanomoles of ^{32}P incorporated per milligram of protein. (26 refs.)

77-5058 **Synthesis and Complete Processing of a High-Molecular-Weight Precursor Polypeptide to Viral Structural Proteins in Toad Oocytes Micro-injected with Avian Myeloblastosis Virus Ribonucleic Acid.** (Eng.) Ghysdael, J. (Dept. Surgery, Duke Univ. Medical Center, Durham, NC 27710); Hubert, E.; Travnicek, M.; Bolognesi, D. P.; Cleuter, Y.; Huez, G.; Marbaix, G.; Portetelle, D.; Chantrenne, H. *Biochem Soc Trans* 5(4): 950-953; 1977.

After micro-injection of *Xenopus laevis* oocytes with avian myeloblastosis virus 60S-70S RNA or its 30S-40S subunits, the major virion structural proteins of the virus were formed by a sequence of posttranslational cleavages of a high molecular wt precursor polypeptide. Toad cells are suitable for use in a model system for the identification and study of proteins coded for by viral messages. (4 refs.)

77-5059 **Single-stranded DNA from Oncornavirus-infected Cells Enriched in Virus-specific DNA**

Sequences. (Eng) Leibovitch, S. A. (Laboratoire de Biologie Moleculaire at Physiopathologie Cellulaire, Groupe de Recherche 8 du C.N.R.S, Institut Gustav-Roussy, 94800 Villejuif, France); Tapiero, H.; Harel, J. *Proc Natl Acad Sci USA* 74(9): 3720-3724; 1977.

Single-stranded (ss) DNA from the leukemic cells of chickens in the terminal stage of leukemia, resulting from avian myeloblastosis (AMV) virus infection, were investigated. These ss DNAs comprised about 2% of the native nuclear DNA. Most of these fragments derived from only one of the DNA double strands; complementary sequences to these fragments were not present in the cell genome. S_1 nuclease digestion revealed that the major part of the AMV complementary (c)DNA synthesized in the presence of actinomycin D (AMD) is ss, while in the absence of AMD, it is double stranded. Almost 50% of the AMV double-stranded cDNA hybridized to ss DNA of productively infected leukemic cells 40 to 50 times faster than to total DNA of the same cells, as compared to 25% for noninfected cells and much less for ss DNA itself. A smaller proportion of ss-cDNA fragments synthesized in the presence of AMD hybridized to ss DNA; and insignificant amounts hybridized to DNA from normal cells as compared to leukemic cells. These findings suggest that actively transcribed DNA sequences can be distributed in the ss DNA fraction. This is probably the result of ss breaks in the vicinity of transcription sites. (44 refs.)

77-5060 **In Vitro Transcription of the Avian Oncornavirus Genome by the RNA-directed DNA Polymerase: Effect of Actinomycin D on the Extent of Transcription.** (Eng) Clayman, C. H. (Dept. Microbiology, Univ. Minnesota Medical Sch., Minneapolis, MN 55455); Collett, M. S.; Faras, A. J. *J Virol* 23(1): 209-212; 1977.

In vitro transcription of the avian oncornavirus genome by RNA-directed DNA polymerase in the presence of actinomycin D (A-D: 100 μg/ml) gave rise to a product DNA capable of protecting 67.4% of the 70S RNA from hydrolysis by pancreatic RNase subsequent to hybridization. This DNA product contained 40.2% duplex DNA. Synthesis of DNA in the absence of A-D yielded a product containing 72.2% duplex DNA that was capable of protecting only 27.0% of the 70S RNA from pancreatic RNase digestion. Thus, the primary effect of A-D on the enzymatic synthesis of DNA from the avian oncornavirus genome by RNA-directed DNA polymerase is the inhibition of duplex DNA formation, resulting in the accumulation of single-stranded minus-strand DNA during synthesis. This action, rather than increasing the extent of genome transcription, is responsible for the more uniform nature of the DNA transcripts synthesized in the presence of A-D. (14 refs.)

77-5061 **Microinjection Analysis of Envelope-Glycoprotein Messenger Activities of Avian Leukosis Viral RNAs.** (Eng.) Stacey, D. W. (Rockefeller Univ., New York, NY 10021); Allfrey, V. G.; Hanafusa, H. *Proc Natl Acad Sci USA* 74(4): 1614-1618; 1977.

Using a microinjection technique, virion RNA from the avian leukosis virus Rous-associated virus 2 (RAV-2) and poly(A)-containing RNA's from RAV-2-infected chick embryo fibroblasts were tested for their ability to direct the synthesis of envelope proteins needed for production of infectious Rous sarcoma virus (RSV) particles. Poly(A)-containing RNA was fractionated by sucrose gradient sedimentation, concentrated, and injected (0.5 × 10^{-10}ml) into 200 fibroblasts transformed by the Bryan high-titer strain of RSV, which is deficient in viral envelope glycoportein. Measurements of infectious RSV released within the first 15 hr revealed that the 21S messenger RNA (mRNA) fractions expressed the greatest activity, with a max rate of release near 9 hr followed by a rapid decline. In contrast, the 35S mRNA fraction expressed only about 3% as much activity. Microinjection of three concentrations of 21S mRNA showed a release of infectious RSV proportional to the injected mRNA concentrations. RAV-2 virion RNA was an inefficient envelope messenger. Injection of both 35S mRNA and 35S virion RNA from RAV-infected cells resulted in a small amount of encapsulated viral particles. (22 refs.)

77-5062 **Transformation of Chicken Embryo Retinal Melanoblasts by a Temperature- sensitive Mutant of Rous Sarcoma Virus.** (Eng) Boettiger, D. (Dept. Anatomy, Univ. Pennsylvania, Sch. Medicine, Philadelphia, PA 19104); Roby, K.; Brumbaugh, J.; Biehl, J.; Holtzer, H. *Cell* 11(4): 881-890; 1977.

The control of normal phenotypic expression was studied in gs- chf- SPAFAS chicken embryo retinal melanoblasts transformed by a temperature-sensitive mutant (tsLA24A) of Prague strain Rous sarcoma virus (RSV). At permissive temperatures (36 C), the cells ceased melanin synthesis, degraded their melanosomes, and released much of the accumulated melanin into the medium. At nonpermissive temperatures (41 C), infected cells assumed an epithelial morphology, actively synthesized melanin, and were difficult to distinguish from normal uninfected controls. Both normal and transformed phenotypes became temperature-dependent in most infected cells. TsLA24A-infected melanoblasts produced virus particles at both temperatures, suggesting that viral synthesis proceeds independently of the host cell's phenotype. (21 refs.)

77-5063 **Transformation of Chondroblasts by Rous Sarcoma Virus and Synthesis of the Sulfated Proteoglycan Matrix.** (Eng) Pacifici, M. (Dept. Anatomy, Univ. Pennsylvania, Sch. Medicine, Philadelphia, PA 19104); Boettiger, D.; Roby, K.; Holtzer, H. *Cell* 11(4): 891-899; 1977.

The control of normal phenotypic expression was studied in chondroblasts transformed by Rous sarcoma virus (RSV). Following proteolysis to remove their extracellular barrier to viral infection, chicken chondroblasts from gs- and chf-SPAFAS embryos were infected and transformed by a temperature-sensitive mutant (tsLA24A) of Prague strain RSV. When grown at permissive temperatures (36 C), the transformed chondroblasts stopped synthesizing their unique type IV sulfated proteoglycan. When the cells were shifted to higher nonpermissive temperatures (41 C), proteoglycan synthesis was reinitiated. These results suggest that the synthesis of sulfated proteoglycans by chondroblasts is promptly and differentially blocked by the RSV viral transformation gene. The existence of a genetic locus that has global control of the cell's phenotypic program is also suggested. (29 refs.)

77-5064 **The Size of Rous Sarcoma Virus mRNAs Active in Cell-free Translation.** (Eng.) Pawson, T. (Dept. Molecular Biology, Univ. California, Berkeley, CA 94720); Harvey, R.; Smith, A. E. *Nature* 268(5619): 416-420; 1977.

The total poly(adenine)-containing cytoplasmic messenger RNA was isolated from Rous sarcoma virus-infected chick cells to examine the mechanism by which RNA tumor virus proteins are synthesized. Two size classes of viral RNA were found in the polysomes of infected cells. A model for the translation of viral RNA is proposed. (38 refs.)

77-5065 **Effect of Low Doses of Actinomycin D on RNA Synthesis in Chick Embryo Fibroblasts Transformed by Rous Sarcoma Virus.** (Eng.) Connan, G. (Laboratoire de Medecine Experimentale du College de France, U 112 de l'I.N.S.E.R.M., 11 Place Marcelin Berthelot - 75231 Paris, Cedex 05, France); Suskind, G.; Rabotti, G. F. *Biochimie* 59(1): 105-109; 1977.

The biochemical characterization of the transcription products of Rous sarcoma virus (RSV)-infected cells during recovery from inhibition by low doses of actinomycin D (A-D) is presented. Primary cultures of chicken embryo fibroblasts from the Edinbourgh Leghorn Brown strain were used. At the time of A-D treatment, the transformed cells comprised 90%-95% of the total infected culture. RNA was labeled with 50 μCi/ml of ^{3}H-uridine. Uninfected cells were used when subconfluent. Cells were exposed to 0.2-0.4 μg/ml A-D for 90 or 180 min and chased for various times. At 0.04 μg/ml and 90 min exposure, the transcription of heterogeneous nuclear RNA and ribosomal RNA in transformed cells occurs 60 min earlier than that in uninfected cells. (23 refs.)

77-5066 **Control of Transformed Focus Morphology in Chicken Cell Cultures Infected with Rous Sarcoma virus.** (Eng.) Diglio, C. A. (Dept. Pathology, Ne York Medical Coll., Valhalla, NY 10595); Dougherty R. M. *J. Gen Virol* 36(3): 413-427; 1977.

Factors that control focus morphology in cell cultures infec ed with the Bryan strain of Rous sarcoma virus (B-RSV) wer examined. Cloning experiments with the round cell and fus form cell variants of RSV confirmed that the two mutar viruses breed true and that these two distinct focus types wer under the control of the virus genome. Three subvariants the round cell focus type failed to breed true in cloning e periments, indicating that this type of focus variation was nc due to virus mutation. Variation in focus morphology wa observed when RSV was plated on chick embryo fibrobla cell lines from different sources, as reflected in the relativ frequency of expression of the three round cell focus type These variations were exhibited between fibroblast cell line of different genetic background, indicating that the ce genome influenced focus expression. Focus expression als varied in fibroblast cell lines from chickens of different age The strongest host influence on focus expression was ob served with fibroblast cell lines derived from selected in dividual tissue of single embryos. The latter two factors (ag and tissue origin) suggested that the differentiated state of th cells also influences RSV focus morphology. (17 refs.)

77-5067 **Glucose Depletion Accounts for the Inductio of Two Transformation-sensitive Membran Proteins in Rous Sarcoma Virus-transformed Chick Embry Fibroblasts.** (Eng) Shiu, R. P. (Lab. Molecular Biology, NCI NIH, Bethesda, MD 20014); Pouyssegur, J.; Pastan, I. *Pro Natl Acad Sci USA* 74(9): 3840-3844; 1977.

The content of plasma membrane proteins with mol wt o 90,000 and 75,000 (GRP-78 and -90) were increased upor Rous sarcoma virus-induced transformation of chick embry fibroblasts (CEF). GRP-90 and GRP-75 content remaine low in the presence of glucose but increased upon withdraw of the glucose. Gel electrophoresis revealed three differen proteins: GRP-78 corresponding to GRP-75, and GRP-9 which could be divided into GRP-95 and GRP-97. In the presence of 24 mM glucose, GRP-78 content was low and GRP-95 was absent. When shifted to a glucose-free medium, GRP-78 and GRP-95 increased while GRP-97 remained the same. Parallel results were observed with the incorporation of ^{35}S-methionine into cellular protein. These changes were then induced in normal cells, proving that the increase was due to glucose depletion and not to transformation alone. The addition of glucose to transformed cells was able to suppress GRP-78 synthesis to the level seen in glucose-fed normal cells. Antisera to GRP-78 indicated that the protein in normal and transformed cells is immunologically the same. (23 refs.)

77-5068 **Proteins of Rous-associated Virus Type 61: Polypeptide Stoichiometry and Evidence That**

Glycoprotein gp35 Is Not a Cleavage Product of gp85. (Eng) Mosser, A. G. (Biophysics Lab., Coll. Agriculture and Life Sciences, Univ. Wisconsin, Madison, WI 53706); Montelaro, R. C.; Rueckert, R. R. *J Virol* 23(1): 10-19; 1977.

The stoichiometry of Rous-associated virus type 61 (RAV-61) polypeptides was determined. Eleven polypeptides were identified, among which were the β(p91) and α(p64) chains of reverse transcriptase. Two minor proteins, p76 and p35, believed to be uncleaved precursors of other core proteins, were also detected. The virions were estimated to contain approx 25 molecules of reverse transcriptase. Chromatographic profiles of the tryptic digests and stoichiometry studies showed that glycoprotein gp35 is not a cleavage product of gp85, and alternative routes of its formation were considered. (40 refs.)

77-5069 **The RNA-dependent DNA Polymerase of Avian Sarcoma Virus B77. Binding of Viral and Nonviral Ribonucleic Acids to the α, β, and $\alpha\beta$ Forms of the Enzyme.** (Eng) Hizi, A. (Dept. Microbiology and Immunology, Duke Univ. Medical Center, Durham, NC 27710); Leis, J. P.; Joklik, W. K. *J Biol Chem* 252(19): 6878-6884; 1977.

The RNA binding affinities of the α, β_2, and $\alpha\beta$ forms of the the avian sarcoma virus B77 RNA-dependent DNA polymerase were examined using a highly sensitive nitrocellulose filter-binding assay. Following DNA polymerase preincubation, tRNATrp formed a complex with the enzyme, yielding identical results with both the α and β_2 forms. Identical results were also obtained when 35 S and 70 S RNA were used instead of tRNATrp. Studies examining binding to tRNATrp, 70 S and 35 S of the Prague subgroup C strain of Rous sarcoma virus (RSV) ribosomal RNA, f2 RNA, 5 S RNA, tRNA lacking tRNATrp, and double stranded RNA revealed that the $\alpha\beta$ form had the greatest affinity to all the single strands tested. The α form had the lowest affinity. A ratio of 1.2 to 6 represented the factor by which the $\alpha\beta$ enzyme affinity exceeded the other two forms; the variation depended on the particular RNA used. The affinity of the $\alpha\beta$ form was greatest for 70 S RSV RNA followed by the 35 S RSV RNA at a 10- to 15-fold decrease. This difference was attributed to the lack of tRNATrp in the 35 S RNA or to differences in the tertiary structure of the molecules. The use of gel filtration experiments confirmed the sensitivity of the nitrocellulose method. These results suggest that while all three forms of B77 DNA polymerase possess affinity for all RNA species, the $\alpha\beta$ form of the enzyme may be functionally most important in vivo. (20 refs.)

77-5070 **Evidence That a Precursor Glycoprotein Is Cleaved to Yield the Major Glycoprotein of Avian Tumor Virus.** (Eng.) England, J. M. (Wistar Inst. Anatomy and Biology, Philadelphia, PA 19104); Bolognesi, D. P.; Dietzschold, B.; Halpern, M. S. *J Virology* 21(2): 810-814; 1977.

A glycoprotein pr90, recognized by anti-gp85 serum, was found in lysates of pulse-labeled transformed cells. Under chase conditions, the level of labeled pr90 was reduced concomitant with the appearance of labeled, cell-associated glycoprotein of B_{77} avian sarcoma virus. (7 refs.)

77-5071 **Nucleotide Sequence at the 5′ Terminus of the Avian Sarcoma Virus Genome.** (Eng.) Shine, J. (Dept. Biochemistry and Biophysics, Univ. California, San Francisco, CA 94143); Czernilofsky, A. P.; Friedrich, R.; Bishop, J. M.; Goodman, H. M. *Proc Natl Acad Sci USA* 74(4): 1473-1477; 1977.

One of the major products of DNA transcription initiated on primer transfer RNA-Trp (tRNA-Trp) located near the 5′ terminus of avian sarcoma virus (ASV) RNA is a DNA chain ($cDNA_{5'}$) complementary to 101 nucleotides of the viral RNA immediately distal to the initiation site. Separation of cleaved DNA fragments by electrophoresis in 20% polyacrylamide gel containing 7 M urea was used to determine (1) the complete sequence of the 101 nucleotides constituting $cDNA_{5'}$ synthesized with Prague subgroup strain C (Pr-C) ASV, and (2) a partial sequence (first 65 nucleotides) for $cDNA_{5'}$ of Bratislava 77 subgroup strain C (B77-C). These two sequences differed at only two positions over the first 65 residues, possibly because of reported differences between their oligopyrimidines. Using the nucleotide sequence of $cDNA_{5'}$ and previous data, a sequence of 119 nucleotides at the 5′ terminus of the Pr-C genome is proposed. Portions of this sequence may be involved in the initiation of translation from the viral gag gene, the binding of ribosomes for initiation, the extension of synthesis from the 5′ to the 3′ terminus, and the integration of viral DNA into the host genome. (32 refs.)

77-5072 **Chicken Macrochromosomes Contain an Endogenous Provirus and Microchromosomes Contain Sequences Related to the Transforming Gene of ASV.** (Eng.) Padgett, T. G. (Dept. Microbiology, Univ. California, San Francisco, CA 94143); Stubblefield, E.; Varmus, H. E. *Cell* 10(4): 649-657; 1977.

Chicken chromosomes from a euploid Marek's lymphoma cell line were partially fractionated according to size by rate zonal centrifugation. DNA-DNA hybridization tests done on resulting DNA indicated that large machrochromosomes harbor the provirus for the endogenous RNA tumor virus of chickens (RAV-O), while a cellular sequence related to the transforming gene of avian sarcoma virus ("sarc" sequence) is located in the microchromosomes. Thus, the RAV-O and sarc components do not appear to be physically linked in chicken DNA and would have to be recombined to generate the virus. (41 refs.)

77-5073 **Application of the Transfection Technique for Segregation of Avian Tumor Viruses.** (Eng) Ogura, H. (Dept. Biochemistry, Cancer Inst., Okayama Univ., Medical Sch., Shikata-cho 2-5-1, Okayama 700, Japan). *Gann* 68(4): 423-426; 1977.

The preparation of infectious DNA for the segregation of progeny viruses by transfection was attempted using a known mixture of viruses. The donor cells for infectious DNA preparation were chick embryo cells (CEC) fully transformed by the B77 strain of avian sarcoma virus (ASV) subgroup C, a mixture of transforming and transformation-defective viruses; and leukemic avian myeloblasts from acutely leukemic chickens inoculated with the BAI-A strain of avian myeloblastosis virus (AMV), a mixture of subgroup A and B viruses. The recipient cells were C/E phenotype of CEC. The $CaCl_2$ method of exogenous DNA uptake was used. About 10 days after transfection, 7/11 CEC treated with B77 ASV DNA showed transformation. The cultures of supernatants of the remaining four cultures showed no transformation 3 wk after transfection, but three were shown to produce transformation-defective virus. No transformation of the AMV cultures was observed 3 wk after transfection, but 6/13 produced a mixture of subgroup A and B viruses, 1 produced only subgroup A, and 3 produced only subgroup B. Thus the transfection technique allows specific virus isolation similar to the classical cloning method. (18 refs.)

77-5074 **Antibody-independent Detection of Virus-specific Glycoprotein Synthesis in Oncornavirus-infected Cells.** (Eng) England, J. M. (Wistar Inst. Anatomy and Biology, Philadelphia, PA 19104); Dietzschold, B.; Halpern, M. S. *J Virol* 23(3): 820-824; 1977.

An antibody-independent method, based on the pulse-labeling of carbohydrate precursors, was developed for the detection of virus-specific glycoprotein synthesis in oncornavirus-infected cells. This method was used to determine whether pr90 was the same as gp90 in chicken embryo cells infected with the B77 strain of avian sarcoma virus. Three approaches were used: the first was to analyze an anti-gp85 immune precipitate, the second was to ascertain whether gp90 could be chased into intracellular DNA as could pr90, and the third was to use chromatographic analysis. It is concluded that the majority of gp90 was equivalent to pr90. This same technique was used in MJD-54 cells (a clone of Moloney leukemia virus-infected JLSV9 cells) to detect an 85,000 dalton glycoprotein that is a possible precursor of gp69/71. These findings indicate that this method can be used to detect synthesis of oncornavirus-specific glycoproteins, even in cases where the virus may be uncharacterized or unknown. (11 refs.)

77-5075 **Relationship Between Feline Leukemia Virus Antigen Expression and Viral Infectivity in Blood, Bone Marrow, and Saliva of Cats.** (Eng) Hoover, E. A. (Dept. Veterinary Pathobiology, Ohio State Univ., Columbus, OH 43210); Olsen, R. G.; Mathes, L. E.; Schaller, J. P. *Cancer Res* 37(10): 3707-3710; 1977.

A $>90\%$ correlation was observed between feline leukemia virus (FeLV) group-specific antigen (GSA) in WBC and viral infectivity (VI) in serum or plasma from 132 cats infected with Rickard strain FeLV, Snyder-Theilen strain feline sarcoma virus (FSV) or field strains of FeLV. Detection of GSA in blood cells was at least as sensitive as detection of VI in serum. In 45% of FeLV GSA-positive cats inoculated with Rickard FeLV, VI was detected in saliva. No saliva samples from GSA-negative cats had VI. Sequential bone marrow biopsies from 34 cats inoculated with Snyder-Theilen FSV indicated that the correlation between FELV GSA in bone marrow cells and blood cells was virtually 100%. In 50% of the cats, FeLV GSA appeared in bone marrow WBC precursors 1 wk before it appeared in peripheral blood WBC. The FeLV GSA-positive state was transient (3-6 wk) in 34% of the Snyder-Theilen FSV-inoculated cats. (21 refs.)

77-5076 **Effect of Interferon on Dimethyl Sulfoxide-stimulated Friend Erythroleukemic Cells: Ultrastructural and Biochemical Study.** (Eng) Luftig, R. B. (Worcester Foundation for Experimental Biology, Shrewsburg, MA 01545); Conscience, J. F.; Skoultchi, A.; McMillan, P.; Revel, M.; Ruddle, F. H. *J Virol* 23(3): 799-810; 1977.

The mechanism of interferon action on dimethyl sulfoxide (DMSO)-stimulated Friend erythroleukemic cells from clone 745 was investigated. Fifty U of mouse interferon in 1.5% DMSO were added to the cells on day 1. After 6 days of this treatment, the minimal effect on growth rate suggested that this quantity of interferon was well below that needed to produce a decrease in proliferative response. Interferon did, however, produce a small, significant increase in Hb production. Interferon effected a rapid decrease in the total number of newly synthesized virus particles in the cells; there was also a parallel decrease in the number of cell sections exhibiting virions. Accumulation of extracellular virus ceased by 5 to 10 hr after treatment. After interferon addition, there was an increase in the number of enveloped A-type particles. These results suggest an inhibition of a late stage of virus maturation as well as inhibition of virus release. There was also an increase in the av number of empty shell particles 12 to 16 hr after treatment; these could represent incomplete products of

us assembly. Cytoplasmic vacuole structures (CVS) de-
eased in parallel with the total virion production. It is sug-
sted that interferon treatment results in a decrease in the
rface area available for viral production and thus in a de-
ease in virus transport. This is coupled with a defect in
aturation leading to more immature forms. There appears
be a decreased synthesis of a viral protein needed in the
VS membrane for virus assembly. (29 refs.)

-5077 **The Friend Virus Genome: Evidence for the Stable Association of MuLV Sequences and Se-
uences Involved in Erythroleukemic Transformation.** (Eng)
ernstein, A. (Ontario Cancer Inst., Toronto, Ontario M4X
K9, Canada); Mak, T. W.; Stephenson, J. R. *Cell* 12(1):
37-294; 1977.

n NIH/3T3 mouse fibroblast culture system was developed
r the propagation of Friend spleen focus-forming virus
SFFV) in excess of its helper virus, lymphoid leukemia virus
LLV). The SFFV harvested from late cell passages of the
riend leukemia virus complex titrated in vivo with multihit
inetics. Hybridization experiments with purified 70S viral
NA and complementary DNA (cDNA) from virus stocks
ontaining an excess of SFFV indicated that 25%-30% of the
DNA represented SFFV-specific sequences. By use of these
irus stocks, several mouse and rat clones nonproductively
nfected with SFFV were isolated. SFFV rescued from these
lones by superinfection with LLV, as well as SFFV produced
y chronically infected NIH/3T3 cells, was subject to restric-
ion by the host regulatory gene *Fv*-2. Each of several SFFV
onproducer clones contained relatively large amounts of vi-
al-specific RNA sequences. Moreover, these clones ex-
ressed high levels of a 15,000 mol wt virion structural pro-
ein, p15, although the levels of the other *gag* gene-coded
roteins and the major viral envelope glycoprotein gp70 were
imilar to those exhibited by uninfected cells. The stable as-
ociation between the erythroleukemic activity of SFFV and
he *gag* gene-coded protein p15 of murine leukemia virus is
liscussed in terms of a possible model for generation of the
SFFV genome. (44 refs.)

7-5078 **Surface Changes in Differentiating Friend Erythroleukemic Cells in Culture.** (Eng.) Eisen, H.
Departement de Biologie Moleculaire, Universite de
Geneve, Geneve, Switzerland); Nasi, S.; Georgopoulous, C.
P.; Arndt-Jovin, D.; Ostertag, W. *Cell* 10(4): 689-695; 1977.

Changes in sensitivity of FL cells to agglutination by plant
ectins were studied during differentiation induced by di-
nethyl sulfoxide, butyric acid or hexamethylene bisaceta-
nide. During the early induction period, there was a great
ncrease in sensitivity to agglutination by all lectins tested for
which the cells have receptors. Later the cells lost this agglutination sensitivity, while receptor number and density increased. (35 refs.)

77-5079 **Solubilized TSTA and the Major Viral Structural Proteins, gp70 and p30, in the Immune Response to Murine Leukemias Induced by Friend and Rauscher Virus.** (Eng) Rogers, M. J. (Lab. Cell Biology, NCI, Bethesda, MD 20014); Law, L. W.; Appella, E.; Oroszlan, S.; Ting, C. C. *Int J Cancer* 20(2): 303-308; 1977.

The role of the viral structural proteins gp70 and p30 in the antitumor immune response was investigated, with particular emphasis upon the relationship between these proteins and the tumor-specific transplantation antigens (TSTA). Antigens present in gp70 and p30 were purified from Rauscher virus and tested in various assays for immunogenicity against lymphocytic leukemias of Friend (FLB-3) or Rauscher virus (RBL-5) origin. Results of in vitro and tumor rejection assays indicate that gp70 and p30 are not major antigens in the immune response. Furthermore, neither protein appeared to be identical to the TSTA present on tumor cell membranes. Although p30 had no effect on either in vitro cytotoxicity or in vivo tumor rejection, gp70 afforded partial protection to mice against subsequent challenge with RBL-5 and FBL-3 leukemias, but only at high concentrations. (24 refs.)

77-5080 **Common Precursor for Rauscher Leukemia Virus gp69/71, p15(E), and p12(E).** (Eng) Karshin, W. L. (Dept. Biology, Univ. Texas System Cancer Center, M. D. Anderson Hosp. and Tumor Inst., Houston, TX 77025); Arcement, L. J.; Naso, R. B.; Arlinghaus, R. B. *J Virol* 23(3): 787-798; 1977.

The synthesis of gp69/71 and p15(E) of Rauscher leukemia virus (RLV) was studied using RLV-infected NIH Swiss mouse embryo cells (JLS-V16) and BALB/c spleen-thymus RLV-infected cells (JLS-V5). The glycoprotein precursor Pr2a+b was found to contain all the tyrosine-containing tryptic peptides of gp69/71 and two additional tryptic peptides found in p15(E). The gene order of the two proteins was found to be $_2$HN-gp69/71-p15(E)-COOH. Tryptic mapping experiments revealed that a protein, p12(E), was related to p15(E). Neither p12(E) nor p15(E) could be phosphorylated, and both could be separated from phosphoprotein p12 chromatographically. p15(E) and p12(E) eluted in the void vol fraction, while p12 eluted between p15 and p10. A sharing of tryptic peptides between p15(E) and p12(E) suggested that p12(E) was derived from p15(E) by proteolytic cleavage. The two p12 proteins could be separated by two-dimensional gel electrophoresis with isoelectric focusing in the first dimension and sodium dodecyl sulfate electrophoresis in the second dimension. (31 refs.)

77-5081 **Identification of Rauscher Murine Leukemia Virus-specific mRNAs for the Synthesis of** ***gag-*** **and** ***env*****-Gene Products.** (Eng.) Van Zaane, D. (Dept. Virology, Central Veterinary Inst., Lelystad, Netherlands) Gielkens, A. L.; Hesselink, W. G.; Bloemers, H. P. *Proc Natl Acad Sci USA* 74(5): 1855-1859; 1977.

Polyadenylated messenger RNA (mRNA) from JLS-V9 cells infected with Rauscher murine leukemia virus (RMLV) was fractionated on the basis of sedimentation velocity. The fractions were translated in vitro in *Xenopus laevis* oocytes, and the products were analyzed immunochemically and electrophoretically for identity with RMLV polypeptides. The 35S mRNA fraction coded for a precursor of the internal or group-specific antigens of the virion (the *gag*-gene products), and the 22S mRNA fraction coded for two viral envelope polypeptides and their precursor polypeptide (*env*-gene products). Synthesis of *gag*- and *env*-related polypeptides did not appear to be coordinated. The results are considered consistent with the AMV-specific mRNA's having open and closed cistrons. (34 refs.)

77-5082 **Sequential Response of Pluripotent and Committed Hematopoietic Colony Forming Cells to Rauscher Leukemia Virus.** (Eng.) Okunewick, J. P. (Viral Oncogenesis Section, Cancer Res. Unit, Allegheny General Hosp., Pittsburgh, PA 15212); Chervenick, P. A. *Proc Soc Exp Biol Med* 155(3): 382-385; 1977.

The temporal relationship of changes in the pluripotent colony-forming cell (CFU-S), the myeloid committed colony-forming cell (CFU-C), and other related hematopoietic parameters were investigated after injection of a low (50 $SED_{50}/_{14}$ units; 50% splenomegalies at 14 days) leukemogenic dose of Rauscher leukemia virus (RLV) in female SJL/J mice. On various days after injection, four animals were sacrificed for analysis of splenic CFU-S and CFU-C content. Samples of tail blood were taken for total WBC and differential counts. The results indicate an action of RLV on both the granulocytic and pluripotent stem cell compartments, with the effects on the pluripotent compartment generally preceding or occurring simultaneously with those seen on the committed granulocytic progenitors, the peripheral white blood compartment, and on spleen size. These results support the hypothesis that, in addition to committed stem cells, pluripotent stem cells are also direct targets of RLV. They suggest that response of the CFU-S is not dependent on previous events occurring in the more differentiated compartments. (24 refs.)

77-5083 **Electron Microscopic Studies of Circular DNA in Mouse Embryo Fibroblasts Infected by Rauscher Leukemia Virus.** (Eng.) Kakefuda, T. (Chemistry Branch, NCI, NIH, Bethesda, MD 20014); Lovinger, G. G.; Gilden, R. V.; Hatanaka, M. *J Virology* 21(2): 792-795; 1977.

Electron microscopic investigation revealed a close circular form of DNA (4.3 μmeter in contour length) in the nucleus of mouse embryo fibroblasts 2.5 hr following infection with Rauscher murine leukemia virus. These circles were distinguishable from mitochondrial DNA by size, absence of secondary features, and resistance to *Eco*RI endonuclease. (14 refs.)

77-5084 **Selective Degradation of Integrated Murine Leukemia Proviral DNA by Deoxyribonucleases.** (Eng) Panet, A. (Dept. Virology, Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel); Cedar, H. *Cell* 11(4): 933-940; 1977.

The accessibility of chromatin-integrated proviral genes was studied using micrococcal nuclease and DNase I. The latter probes are specific for active genes in the open regions of chromatin, and they more readily digest proviral sequences in active virus producers than in cells that do not produce mature virus particles. Thus, in NIH Swiss mouse cells infected with Moloney murine leukemia virus (M-MuLV), >80% of the endogenous DNA sequences were found in the open (active) regions of chromatin, but only one-third were resistant to nuclease. In uninfected Swiss mouse cells, endogenous proviral sequences were distributed randomly with respect to nuclease digestion. This implies that infection by an exogenous virus can affect the nuclease sensitivity of endogenous sequences that were present prior to infection. In rat cells infected with M-MuLV, the amount of proviral DNA sensitive to pancreatic DNase I was three to five times higher in actively dividing cells than in cells arrested at the G_0 phase. These results suggest that the relative positions of chromatin proteins and proviral sequences also depend upon the cell cycle phase, and they may explain the reduced production of virus particles at certain phases. (23 refs.)

77-5085 **Mechanism of Murine Leukemia Virus-induced Fusion in Rat Myoblasts Defective in Differentiation.** (Eng) Wong, P. K. (Dept. Microbiology and Sch. Basic Medical Sciences, Univ. Illinois, Urbana, IL 61801); Yuen, P. H.; Kaufman, S. J. *J Virol* 23(3): 768-775; 1977.

Moloney murine leukemia virus (Mo-MLV) was used to induce fusion of fu-1 cells, a line of rat myeloblasts defective in differentiation. Heating the virus at 56 C for 30 min inhibited syncytium formation. Varying doses of UV irradiation decreased infectivity $>10^5$-fold, but decreased fusion by only about 10-fold, suggesting that noninfectious virus can still form syncytia. Treatment of Mo-MLV with anti-MLV antiserum arrested fusion for only about 5 min, during which time the virus presumably adsorbed and penetrated into the cell. When fu-1 cells were incubated with the *ts3* temperature-sensitive Mo-MLV mutant at the nonpermissive temperature (39 C), budding virions accumulated on the cell membrane, but mere contact was not sufficient to cause cell fusion. Fusion occurred at the permissive temperature (34 C), indicating that complete virions are required. Treatment of cultures with actinomycin D (2 μg/ml) or cycloheximide (100 μg/ml) had no effect on cell fusion. Thus, neither cellular nor viral RNA and protein syntheses are required for fusion. Results suggest that adsorption and penetration may initiate an alteration in the cell membrane that leads to cell fusion. (16 refs.)

77-5086 **Expression of an Antigen Similar to Gross Virus on the Surface of Leukemic Cells of C57BL/6 Mice Infected by Radiation Leukemia Virus.** (Fre) Gerlier, D. (Laboratoire d'Immunologie, Centre Leon-Berard, 28, rue Laennec, 69373 Lyon Cedex 2, France); Guillemain, B.; Dore, J. F.; Duplan, J. F. *C R Acad Sci [D] (Paris)* 284: 2431-2434; 1977.

A leukemogenic viral complex was demonstrated in cultures of 13-3-C cells derived from a radiation leukemia virus (RadLV-Rs)-induced tumor in C57BL/6 mice. The 13-3-C virus was shown to be a complex form of an ecotropic B and xenotropic virus. Injection of 13-3-C virus into C57BL/6 mice had the same pathogenic effects as RadLV-Rs, and it provoked the appearance of specific antigens on the surface of infected leukemic cells that were partially or totally identical to Gross leukemia virus (GCSAa). Molecular hybridization experiments with complementary DNA showed that the 13-3-C virus acts similarly to murine endogenous ecotropic viruses. (14 refs.)

77-5087 **Relationship Between Endogenous Ecotropic Murine Leukemia Virus and Radiation Leukemogenesis in Various Strains of Mice.** (Eng.) Takamori, Y. (Radiation Center Osaka Prefecture, Shinke-cho, Sakai, Osaka, Japan); Okumoto, M.; Iwai, Y.; Iwai, M. *Annu Rep Radiat Center Osaka* 17: 77-80; 1976.

The relationship between the incidence of radiation-induced leukemia and replication of infectious ecotropic leukemia virus was investigated using RF, BALB/c, NIH Swiss, and DD/Tb mice. The animals were exposed to four doses of 170 R at weekly intervals, starting when they were 4 wk old. All the mice had a high susceptibility to the induction of leukemia by fractionated x-irradiation. Most of the leukemias induced were thymic lymphomas. The replication of endogenous ecotropic murine leukemia virus (MuLV) was enhanced by x-irradiation in RF and BALB/c mice, but no ecotropic virus could be detected in NIH Swiss or DD/Tb mice. There are two possible explanations of these results from the viewpoint of viral etiology. First, certain viruses, such as xenotropic ones that could not be detected by the XC plaque test used for the MuLV assay may be activated by x-irradiation and may cause leukemia. Second, an infectious virus particle may not be required in the induction of leukemia. Expression of a part of the virus genome may be enough for leukemogenesis, as suggested by the oncogene theory. (12 refs.)

77-5088 **Identification of Mouse Chromosomes Required for Murine Leukemia Virus Replication.** (Eng) Gazdar, A. F. (NCI-VA Medical Oncology Branch, Veterans Admin. Hosp. and NCI, Washington, DC 20422); Oie, H.; Lalley, P.; Moss, W. W.; Minna, J. D. *Cell* 11(4): 949-956; 1977.

The replication patterns of seven strains of murine leukemia virus (MuLV) were studied in 41 Chinese hamster x mouse hybrid primary clones. Ecotropic and amphotropic strains of MuLV replicated in mouse and some hybrid cells, but not in hamster cells, indicating the need for dominantly expressed mouse cellular genes. The replication patterns for each of the five ecotropic and both of the amphotropic strains were similar. The patterns of these two MuLV classes indicated that different mouse chromosomes were required for their replication. Chromosome and isozyme analysis assigned to mouse chromosome 5 a gene (*Rec-1*) that is necessary and may even be sufficient for ecotropic virus replication. The possibility that chromosomes 15 and 17 may also be necessary but insufficient for ecotropic virus replication was not excluded. Another gene (*Ram1-1*), which is necessary and possibly sufficient for amphotropic virus replication, was assigned to mouse chromosome 8. Chromosome 19 could not be excluded as being independent of amphotropic virus replication, and the possibility that chromosomes 7, 12, 15, 16, and 17 are necessary but insufficient could not be ruled out. The assignment of the *Fv-1* locus to chromosome 4 was confirmed, and the ability of hybrid cells, which have segregated mouse chromosome 4 but retained chromosome 5, to replicate N- and B-tropic strains of MuLV was established. (34 refs.)

77-5089 **Genetic Studies of the *Fv-1* Locus of Mice: Linkage with *Gpd-1* in Recombinant Inbred Lines.** (Eng) Taylor, B. A. (Jackson Lab., Bar Harbor, ME 04609); Bedigian, H. G.; Meier, H. *J Virol* 23(1): 106-109; 1977.

Multiple recombinant inbred mouse lines derived from crosses between strains permissive to N-tropic murine leukemia viruses (*Fv-1n*) and strains permissive to B-tropic murine leukemia viruses (*Fv-1b*) were characterized as to *Fv-1* genotype and other chromosome 4 markers, including the closely linked hexose-6-phosphate dehydrogenase isozyme locus (*Gpd-1*). Among the 45 lines tested, only one recombinant between *Fv-1* and *Gpd-1* was found. No results suggestive of any genetic alteration, such as intragenic or unequal crossing-over involving *Fv-1*, or mutation were seen. None of the lines was either resistant or susceptible to both N- and B-tropic viruses. The *Fv-1* locus was characterized for 19 other inbred strains. (24 refs.)

77-5090 **Characterization of Purely Ecotropic and Amphotropic Naturally Occurring Wild Mouse Leukemia Viruses.** (Eng) Rasheed, S. (Dept. Pathology, Univ. Southern California Sch. Medicine, 1840 N. Soto St., Los Angeles, CA 90032); Toth, E.; Gardner, M. B. *Intervirology* 8(6): 323-335; 1977.

Two new strains of murine leukemia virus (MuLV), one (strain 4996) purely ecotropic and the other (strain 1313) purely amphotropic, were isolated from spontaneous lymphomas in aged wild mice, *Mus musculus*. Both strains exhibited general properties of the MuLV group, including typical C-type morphology, a density of 1.14-1.16 g/cm^3, RNA-directed DNA polymerase activity, six major internal polypeptides, and the MuLV-specific, p30 antigen. Each isolate also had the ability to rescue the sarcoma genome from murine sarcoma virus-transformed nonproducer cells. The host range of 4996 virus was restricted to murine cells, and it was further characterized by N-tropism. Neutralization interference and XC test properties established 4995 virus as a new virus. Strain 4996 virus induced lymphoma but no paralysis after 10 mo in 6/25 NIH Swiss newborn mice. The 1313 virus showed N- and B-tropism, depending upon the test cells. Strain 1313 is the only MuLV that replicates in chicken cells. Although strain 1313 virus did not, after 8 mo, produce any disease in 8 NIH Swiss mice or 17 BALB/c mice, it was infective for NIH Swiss mice but not BALB/c mice, based upon serum virus isolation at 2 mo of age. (38 refs.)

77-5091 **Evidence for Recombination Between N- and B-tropic Murine Leukemia Viruses: Analysis of Three Virion Proteins by Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis.** (Eng) Schindler, J. (Center Cancer Res., Massachusetts Inst. Technology, Cambridge, MA 02139); Hynes, R.; Hopkins, N. *J Virol* 23(3): 700-707; 1977.

Sc-1 cells were infected with each of 21 clonal isolates of XLP-N C-type viruses (large XC plaque-forming N-tropic recombinants) obtained from seven independent crosses between an N-tropic virus that makes small XC plaques (SP-N) and a B-tropic virus that makes large XC plaques (LP-B). Both parent viruses were derived from BALB/c mice. Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis revealed that three viral proteins, p15, p30, and gp70 (the major envelope glycoprotein), of the parental viruses differed in electrophoretic mobility. All 21 recombinants possessed a p30 that comigrates with the p30 of SP-N. Thus, N- or B-tropism might be determined by p30 or a closely linked gene. Of the 21 viruses studied, 16 possessed a gp70 that migrates like the gp70 of LP-B and 2/21 possessed a p15 comigrates with the p15 of LP-B. These results indicate that XLP-N viruses are genetic recombinants. Possible biological implications of the data are discussed. (30 refs.)

77-5092 **Two Distinct Endogenous Type C Viruses Isolated from the Asian Rodent *Mus cervicolor*: Conservation of Virogene Sequences in Related Rodent Species.** (Eng.) Benveniste, R. E. (Lab. Viral Carcinogenesis, NCI, Bethesda, MD 20014) Callahan, R.; Sherr, C. J.; Chapman, V.; Todaro, G. J. *J Virol* 21(3): 849-862; 1977.

The cocultivation of a lung cell line from the Southeast Asian mouse *Mus cervicolor* with cells from heterologous species resulted in the isolation of two new distinct C-type viruses. Both viruses are endogenous to *M. cervicolor* and are present in multiple copies in the cellular DNA of these mice. One of the viruses, designated *M. cervicolor* C-type, replicates readily in SIRC rabbit cells and is antigenically related to the infectious primate C-type viruses isolated from a woolly monkey (simian sarcoma-associated virus) and gibbon apes (gibbon ape leukemia virus). This virus is also closely related by both immunological and nucleic acid hybridization criteria to a C-type virus previously isolated from a second Asian murine species, *M. caroli*. The isolation of the *M. cervicolor* CI-type virus thus provides further evidence that the infectious primate C-type viruses originated by transspecies infection of primates by an endogenous virus. The second virus, designated *M. cervicolor* CII-type, replicates well in various cell lines derived from the laboratory mouse *Mus musculus*. Although antigenically related to the C-type viruses of *M. musculus*, the *M. cervicolor* CII-type virus isolate can be readily distinguished from standard murine leukemia viruses. Both new C-type viruses from *M. cervicolor* are unrelated to the retrovirus (M432) isolated from the same *Mus* species. The DNA of *M. cervicolor*, therefore, contains multiple copies of at least three distinct classes of endogenous viral genes. An examination of the cellular DNA of other rodent species for nucleic acid sequences related to the genomes of both *M. cervicolor* CI- and CII-type revealed that both viruses have been highly conserved evolutionarily and that rodent species, such as laboratory mice and rats, contain endogenous virogenes related to those in the DNA of *M. cervicolor*. (53 refs.)

77-5093 **Analysis of Murine C-Type Virus Structural Proteins by Rocket and Crossed Immunoelectrophoresis.** (Eng.) Georgiades, J. A. (Dept. Human Biology, Rega Inst., Univ. Leuven, B-3000, Leuven, Belgium); Billiau, A.; Verbruggen, R.; De Somer, P. *J Immunol Methods* 17(1/2): 177-187; 1977.

Laurell rocket and crossed immunoelectrophoresis revealed

15 precipitin lines in crude virus concentrates prepared from the supernatant of cells chronically infected with Rauscher murine leukemia virus. By using monospecific reference antisera, four of these lines were identified as p30, p15, p12, and p10. Several lines also reacted to anti-gp 69/71, indicating the possible presence of viral precursor proteins. (9 refs.)

77-5094 **Enhanced Oncogenicity of Tumor Cells Spontaneously Producing Endogenous Murine 'C' Type Virus (Meeting Abstract).** (Eng) Axler, D. A. (Pennsylvania Coll. Podiatric Medicine, Philadelphia, PA 19107). *In Vitro* 13(3): 158; 1977. (no refs.)

77-5095 **C-Type Virus Particles in the Transplantable Mouse Bladder Tumour FCB Grown In Vitro.** (Eng) Flaks, A. (Cancer Unit, Dept. Biology, Univ. York, Heslington, York, England). *Cancer Lett* 3(1-2): 65-70; 1977.

Electron microscopic studies of the transitional cell tumor line FCB, a transplantable murine bladder tumor induced by dibutylnitrosamine, revealed the presence of C-type virus particles in the in vitro cultures obtained from the 20th, 34th, and 42nd transplant generations. Many of the particles were in the process of budding into cytoplasmic vacuoles, although no immature virus or precursors on A-type particles were seen. Also, the in vitro cultures FCB cells, in comparison with both the cells of origin and those of the solid tumor, showed a high degree of morphological simplification, which is common to most highly malignant neoplasms and is associated with a loss of specialized functions. The possible relation of the virus to murine bladder carcinogenesis is discussed. (14 refs.)

77-5096 **Occurrence of Mixed Forms of Intracisternal Virus-like Particles in Somatic Hybrid Cells.** (Eng.) Yotsuyanagi, Y. (Centre de Genetique Moleculaire du C.N.R.S., 91190 Gif-sur-Yvette, France). *J Ultrastruct Res* 60(1): 71-83; 1977.

Various types of mixed forms of intracisternal particles in hamster x mouse somatic hybrid cells were examined by electron microscopy. Seven hybrids from four independent crosses of hamster melanoma cells with mouse fibroblast or melanoma cells were studied. The somatic hybrid cells carried mixed populations of A- and R-type virus-like particles within the cisternae of the endoplasmic reticulum. Some hybrids also produced intracisternal particles of immature C (also called enveloped A) morphology. These three morphologically distinct intracisternal particles elaborate two types of mixed structure: (1) aggregates of two or more complete particles of different types enclosed within a common envelope; and (2) structures that appear to be single particles but simultaneously contain nucleoid materials of two different types. Since the nature of intracisternal particles remains unclear, it is difficult to assess the biological significance of the formation of mixed structures between them. However, these findings may help in understanding the heterozygosis frequently observed in the genetic study of RNA viruses that mature by budding at the surface membrane of animal cells. Both simultaneous occurrence of two types of mixing and the predominant or exclusive occurrence of one type appear conceivable as a structural basis for heterozygosis. (27 refs.)

77-5097 **Iododeoxyuridine Activation of Oncornavirus-like Particles of Hamster Origin (Letter to Editor).** (Eng.) Yaniv, A. (Dept. Human Microbiology, Sackler Sch. Medicine, Tel Aviv Univ., Tel Aviv, Israel); Eylan, E. *Br J Cancer* 36(3): 397-399; 1977.

Oncornavirus-like particles in a spontaneously transformed cell line (Clone B) were activated after 24 hr incubation at 37 C with 30 μg/ml 5-iododeoxyuridine. Max release of particles occurred after 48-72 hr and then declined sharply. Investigations are underway to ascertain the biological activities of these particles. (11 refs.)

77-5098 **Intracytoplasmic Type A Particles in Viper Spleen Cells.** (Eng.) Lunger, P. D. (110 Wolf Hall, Newark, DE 19711); Clark, H. F. *J Natl Cancer Inst* 58(3): 809-811; 1977.

Structures resembling typical type A particles were seen in paranuclear inclusions in cultured C-type particle-producing viper cells. Both the incidence and size of the inclusions were slightly increased when cells were treated with 1 μg/ml ethidium bromide. Chloramphenicol did not produce this effect. This the first report of type A particles in poikilothermic vertebrate cells. (16 refs.)

77-5099 **Identification of the Structural Proteins of the Murine Mammary Tumor Virus That Are Serologically Related to the Antigens of Intracytoplasmic Type-A Particles.** (Eng.) Sarkar, N. H. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021); Whittington, E. S. *Virology* 81(1): 91-106; 1977.

The immunological relationships between intracytoplasmic murine mammary tumor virus (MuMTV) particles A and B were investigated to determine whether A particles are the preformed cores of mature B particles. Extracts from murine tumors containing A and B particles and from tumors containing only A particles produced A-particle-associated antigens in immunodiffusion tests with rabbit antisera. Rabbit anti-MuMTV serum precipitated all the major polypeptides of MuMTV (gp55, gp36, p28, p18, and p12) when reacted with solubilized MuMTV proteins. Rabbit anti-A particle serum precipitated only p28, p18, and p12. Polyacrylamide gel electrophoresis of MuMTV proteins precipitated by goat anti-MuMTV gp55 or by p28 sera showed only gp55 or p28. The specificity of these reactions was demonstrated by the fact that neither normal goat nor rabbit serum precipitated detectable amounts of viral proteins. These results suggest that A particles contain antigens that cross-react with all three major internal proteins of MuMTV. They support the hypothesis that intracytoplasmic A particles are the preformed cores of B particles. (41 refs.)

77-5100 **Nutritional Factors That Influence Expression of Mouse Mammary Tumor Virus: Iron, Zinc and Lipids (Meeting Abstract).** (Eng) Nagle, S. C. (NCI Frederick Cancer Research Center, P. O. Box B, Frederick, MD 21701); Fine, D. L.; Kmetz, J. P. *In Vitro* 13(3): 173; 1977. (no refs.)

77-5101 **Isolation of the Mouse Mammary Tumor Virus Sequences Not Transmitted as Germinal Provirus in the C3H and RIII Mouse Strains.** (Eng.) Drohan, W. (Meloy Labs., Springfield, VA 22151) Kettmann, R.; Colcher, D.; Schlom, J. *J Virol* 21(3): 986-995; 1977.

Radioactive 60-70S RNA from the mouse mammary tumor virus (MMTV) produced by a C3H mouse early mammary tumor cell line (Mm5mt) hybridized to a greater extent, and at a lower $C_0T1/2$ value, to the DNA of C3H mammary tumor cells than to the DNA of C3H liver cells. The ^{125}I-labeled MMTV(C3H) 60-70S RNA was annealed to a vast excess of DNA from C3H livers, and single-stranded RNA was eluted from hydroxylapatite and recovered. This recycled RNA did not hybridize to the DNA of the apparently normal organs tested from normal or mammary tumor-bearing C3H mice, but it hybridized extensively to the DNA from the C3H mammary tumor cell line and the DNA from spontaneous C3H mammary tumors. This hybridization was prevented by the addition of unlabeled MMTV 60S-70S RNA but was unaffected by the addition of unlabeled 60-70S RNA of C3H C-type virus. Similar experiments on RIII mice indicated that, as in C3H mice, the MMTV sequences in the DNA of early RIII mammary tumors are transmitted by mechanisms other than via the germ line. These studies further defined the differences between early and late MMTV in both C3H and RIII mice. (30 refs.)

77-5102 **Multiple Antigenic Determinants on the Major Surface Glycoprotein of Murine Mammary Tumor Viruses.** (Eng) Teramoto, Y. A. (Div. Life Sciences, Meloy Labs., Springfield, VA 22151); Kufe, D.; Schlom, J. *Proc Natl Acad Sci USA* 74(8): 3564-3568; 1977.

Competitive radioimmunoassays (CRI's) for the whole mouse mammary tumor virus (MMTV) virion and for purified MMTV polypeptides were used to study antigenic similarities or differences among MMTV's from three different mouse strains, C3H, RIII, and GR. CRI's with externally labeled (^{125}I) virion preparations indicated that virions from the three strains competed identically in group-specific assays but not in the appropriate type-specific assays. No significant qualitative differences were observed whether virion preparations from mouse milk or tissue culture fluid were used. Similar results were obtained when preparations of the major external protein of MMTV's, a glycoprotein of mol wt 52,000 (gp52), were used as competitors. MMTV's of RIII, C3H, and GR mice, grown in feline cells, competed similarly to the corresponding murine-derived MMTV's, demonstrating that the type- and group-specific antigenic reactivities are viral-coded. CRI's demonstrated two kinds of type-specific reactions: complete cross reactions between MMTV (C3H) and MMTV (RIII). These results indicate that MMTV's derived from different mouse strains contain both type- specific and group-specific reactivities, both of which are associated with gp52. (25 refs.)

77-5103 **Synthesis and Distribution of Vesicular Stomatitis Virus-specific Polypeptides in the Absence of Progeny Production.** (Eng.) Little, S. P. (Dept. Microbiology and Molecular Genetics, Harvard Medical Sch., Boston, MA 02115); Huang, A. S. *Virology* 81(1): 37-47; 1977.

Infectious progeny formation was inhibited, and the distribution of viral polypeptides in the cellular, virion-associated, and soluble fractions of Chinese hamster ovary cells infected by vesicular stomatitis virus (VSV) was then examined to determine whether or not the soluble polypeptides resulted from virion degradation. When the cells were coinfected with standard infectious particles plus defective interfering particles or when cells were infected under nonpermissive conditions, synthesis of virus-specific RNA was reduced 80% without affecting the appearance of soluble viral polypeptides. Cell-associated polypeptides were also present in normal amounts. Use of the glycoprotein mutant *ts*045 indicated the absence of virion maturation and enhanced the appearance of soluble viral polypeptides. The major soluble viral polypeptide was a glycoprotein that migrated more rapidly than the virion-associated glycoprotein. These results indicate that the distribution of viral proteins in cell-associated and extracellular soluble fractions is independent of the production of infectious progeny. They suggest that the interaction between the outer envelope-associated viral glycoprotein G and the inner envelope-associated matrix protein M exists in three different states: an initial very unstable association; possible stabilization at the cell surface via interactions with another viral membrane matrix protein; and the aggregation of G at the cell surface initited by nucleocapsids interacting through the two matrix proteins. The first two stages of this interaction probably result in the shedding of G from the cell surface. (25 refs.)

77-5104 **Factors Affecting Composition and Thermostability of Mengovirus Virions.** (Eng.) Bond, C. W. (Dept. Pathology, Univ. California at San Diego, La Jolla, CA 92093) Swim, H. E. *J Virol* 21(3): 1256-1261; 1977.

L-67-S cells, a substrain of L929 mouse fibroblasts, were infected with mengovirus at 20 plaque-forming units/ml medium. The composition of mengovirus virions produced by the infected cells varied with incubation temperature. Virions produced at 37.0 or 39.5 C contained four major polypeptides (α, β, γ and δ) and one minor polypeptide (β'). Virions produced at 31.5 C contained two additional polypeptides (D_1 and E). The virions of two temperature-sensitive (ts) and thermolabile mutants of mengovirus (ts) and thermolabile mutants of mengovirus (ts25 and ts88) contained an increased amount of polypeptide β', with a corresponding decrease in polypeptide β when compared with wild-type mengovirus. (15 refs.)

77-5105 **Inhibition of In Vitro Lymphoproliferative Responses by In Vivo Passaged Rat 13762 Mammary Adenocarcinoma Cells. II. Evidence that Kilham Rat Virus is Responsible for the Inhibitory Effect.** (Eng) Campbell, D. A. (Lab. Immunodiagnosis, NCI, Building 10, Room 8B11, Bethesda, MD 20014); Staal, S. P.; Manders, E. K.; Bonnard, G. D.; Oldham, R. K.; Salzman, L. A.; Herberman, R. B. *Cell Immunol* 33(2): 378-391; 1977.

Kilham rat virus (KRV) was isolated from a lymphocyte cytopathic 13762 summary adenocarcinoma tumor line maintained in Fischer rats and from three other in vivo passaged rat tumors maintained in the same animal room. However, the virus could not be isolated from a noncytopathic (C58NT)D tissue culture line. In tests using $CsCl_2$-purified KRV preparations, the virus replicated in rat lymphocytes and profoundly depressed lymphocyte viability and lymphoproliferative responses. Heterologous anti-KRV antiserum reversed the inhibitory effects of the purified virus preparation and the inhibitory effects of ultrasonically disrupted KRV-infected tumor cells, but it only partially reversed the inhibitory properties of x-irradiated whole 13762 tumor cells. The results suggest that KRV may account for some, if not all, of the inhibitory properties of the 13762 tumor line. (28 refs.)

77-5106 **Isolation of Intracellular Replicative Forms and Progeny Single Strands of DNA from Parvovirus KRV in Sucrose Gradients Containing Guanidine Hydrochloride.** (Eng.) Lavelle, G. (Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN 37830); Li, A. T. *Virology* 76(1): 464-467; 1977.

DNA extracted from purified Kilham rat viruses by guanidine HCl appeared to consist of DNA complexed with protein that contributed to the formation of circular molecules. The complexed DNA had a sedimentation rate different from that of protease-detergent-extracted viral DNA. There was no evidence of bound protein. (19 refs.)

77-5107 **Evidence for Terminal S_1-Nuclease-resistant Regions on Single-stranded Linear DNA.** (Eng.) Salzman, L. A. (Dept. Health, Education, and Welfare, NIH, Bethesda, MD 20014). *Virology* 76(1): 454-458; 1977.

Experimental evidence suggests that the 5′ and probably the 3′-termini of the single-stranded DNA from the Kilham rat virus are S_1 nuclease-resistant and that they elute from cellulose columns as double-stranded DNA. These double-stranded termini could result from hairpin turns of terminal palindromic sequences. The 3′ double-stranded DNA end of the molecule may serve as a primer for the replication of linear, single-stranded DNA. (18 refs.)

77-5108 **The Autoradiographic Pattern of DNA Synthesis in Papova Virus- and N-Methyl-N-nitroso Urea (MNU)-induced Skin Tumors of the Syrian Hamster (*Mesocricetus auratus*).** (Eng.) Amlacher, E. (Pathologisches Institut der Friedrich-Schiller-Universitat, Ziegelmuhlenweg 1, DDR-69 Jena, E. Germany); Bierwolf, D. *Exp Pathol (Jena)* 13(2-3): 88-100; 1977.

An autoradiographic study was made of the nature of DNA synthesis in tumors induced in the skin of Syrian hamsters by papovavirus or by methylnitrosourea (MNU). Most of the DNA synthesis in the virus-induced tumors was demonstrated to be of cellular origin. Progressive virus multiplication was only seen in cells adjacent to the keratinizing regions of the tumors. Cells active in DNA synthesis were also seen in the keratinizing regions of MNU-induced tumors. The pattern of DNA synthesis in these tumors varied with increasing malignancy, and DNA synthesis could also be seen in cells outside of the basal strata. (9 refs.)

77-5109 **Mechanism of Purine Nucleoside Handling and Transport in Isolated Membrane Vesicles from Polyoma Transformed BHK/21 Cells.** (Eng) Dowd, D. J. (Dept. Biology, State Univ. New York, Albany, NY 12222); Quinlan, D. C.; Hochstadt, J. *Biochemistry* 16(20): 4526-4532; 1977.

The mechanism of inosine uptake into membrane vesicles prepared from baby hamster kidney (BHK) cells was examined. Two distinct processes were observed, either purine nucleoside phosphorylase (PNP)-dependent (in which inosine was cleaved) or PNP-independent. The PNP-dependent mechanism involved the accumulation of ribose 1-phosphate (ribose-1-P) while hypoxanthine was left in the medium; the ribose-1-P had a low Km and a high initial rate. The PNP-independent mechanism resulted in the intravesicular accumulation of intact inosine metabolized by a PNP activity; this enzyme may or may not be the same as that used in the first mechanism. The initial rate and Km of the two mechanisms were distinct. The PNP-dependent mechanism was more sensitive to inhibition by N-ethylmaleimide and adenine. The steady-state level of substrate accumulation was the same in both mechanisms. Adenosine was also taken up by the vesicles, but kinetic data indicated that adenosine and inosine were probably not taken up by the same vesicles. Data for subfractionation of the plasma membrane are provided with respect to enzyme function as well as transport function. It is concluded that a variety of nucleoside transport mechanisms are available to mammalian cells and that a single cell line can exhibit alternative transport modes. (17 refs.)

77-5110 **Alterations of Neoplastic Characteristics of a Glutamine-independent Variant (GIV) of Polyoma-BHK (Meeting Abstract).** (Eng) Gammon, M. T. (Massachusetts General Hosp., Boston, MA 02114); Isselbacher, K. J. *In Vitro* 13(3): 172; 1977. (no refs.)

77-5111 **Amount and Distribution of Virus-specific Sequences in Giant RNA Molecules Isolated from Polyoma-infected Mouse Kidney Cells.** (Eng.) Lev, Z. (Dept. Biology, Technion-Israel Inst. Technology, Haifa, Israel) Manor, H. *J Virol* 21(3): 831-842; 1977.

The composition of giant RNA molecules, synthesized in mouse kidney cells late in productive infection by polyoma virus, was studied by a two-step hybridization procedure with polyoma DNA. Giant molecules longer than a complete transcript of the polyoma genome were purified from cells that had been pulse-labeled for 30 min with ^{3}H-uridine and annealed, under mild conditions (50% formamide, 37 C), with polyoma DNA loaded on nitrocellulose filters. Hybridized RNA, 4%-7% of the entire population of ^{3}H-labeled molecules and up to 15% of the molecules containing polyadenylic acid [poly(A)], was eluted and annealed a second time with polyoma DNA under more stringent conditions. In this second step, 75% of the ^{3}H-labeled RNA formed an RNase-resistant hybrid. Under the same conditions, up to 80% of complementary RNA hybridized with polyoma DNA. Since the difference between 75% and 80% is within the experimental error of the hybridization assays, the results suggest that the giant molecules selected by the first hybridization consist entirely of virus-specific sequences or contain, at the most, a minor fraction of nonviral sequences. To examine the possibility that these nonviral sequences are clustered at the 3′-terminus of these molecules, poly(A)+ giant RNA, which had not been preselected by hybridization with polyoma DNA, was fragmented by a limited alkaline hydrolysis. Fragments linked to the poly(A) segment were separated from the rest of the cleavage products. A one-step hybridization with polyoma DNA revealed that both fractions contain 8%-10% of virus-specific sequences. These results indicate that the 3′-termini of the poly(A) + polyoma-specific giant RNA molecules consist of viral rather than nonviral sequences. (33 refs.)

77-5112 **Histotypic Interactions of Normal and Neoplastic Salivary Epithelium (Meeting Abstract).** (Eng) Dawe, C. J. (NCI, Bethesda, MD 20014); Morgan, W. D.; Williams, J. E.; Summerour, J. P. *In Vitro* 13(3): 179; 1977. (no refs.)

77-5113 **DNA-binding Proteins in Mouse Cells Infected with Polyoma Virus.** (Eng.) Clertant, P. (Centre de Biochimie, Universite de Nice, Parc Valrose, Nice, France); Blangy, D. *Intervirology* 8(1): 44-51; 1977.

DNA-cellulose chromatography and sodium dodecyl sulfate-polyacrylamide gel electrophoresis were used to isolate and compare DNA-binding proteins from uninfected or polyoma virus-infected murine 3T6 cells. Four major new polypeptides with molecular wts of approx 160,000, 130,000, 86,000, and 81,000 were detected in infected cells. The last two were compatible with previous estimates of the molecular wt of polyoma T antigen. (28 refs.)

77-5114 **Locomotory Behavior, Contact Inhibition, and Pattern Formation of 3T3 and Polyoma Virus-transformed 3T3 Cells in Culture.** (Eng) Bell, P. B. (Dept. Biology, Univ. California at Los Angeles, Los Angeles, CA 90024). *J Cell Biol* 74(3): 963-982; 1977.

The behavior of 3T3 cells and 3T3 cells transformed by polyoma virus (Py3T3) was examined using time-lapse cinemicrography to determine what factors are responsible for the marked differences in the patterns formed by the two cell lines in culture. Py3T3 cells exhibited basically the same types of contact interactions as their nontransformed parent cells. Contact between cells of both types resulted either in the cessation of locomotion in the direction that produced the contact or in the continued movement of one cell under another. In Py3T3 cells, the crisscross pattern seen in cell culture was due exclusively to underlapping rather than overlapping, as had been previously assumed. Both cell types, after contact between lamellipodia, showed inhibition of locomotory activity and adhesion formation. The two cell types, however, did show quantitative differences in the frequency of underlapping, the frequency with which contact results in inhibition of locomotion, and the proportion of the cell margin that adheres to the substratum. The increased frequency of Py3T3 underlapping was correlated with the reduced frequency of substratum adhesions, which in turn favors underlapping. It is concluded that the differences in culture patterns are the result of differences in the shapes of the individual cells, such that underlapping and, hence, crisscrossing are favored in Py3T3 cells but discouraged in 3T3 cells. The results suggest that the invasiveness of malignant cells in vivo results not from cells crawling over each other, but from infiltration along available noncellular substrata. (59 refs.)

77-5115 **Immediate Glycosylation of Sindbis Virus Membrane Proteins.** (Eng.) Sefton, B. M. (Tumor Virology Lab., Salk Inst., Post Office Box 1809, San Diego, CA 92112). *Cell* 10(4): 659-668; 1977.

The mechanism by which the membrane proteins of Sindbis virus are initially glycosylated during their growth in chick cells was examined. The two viral proteins are apparently glycosylated before release from the polysome, involving transfer of a large 1,800-dalton oligosaccharide to the polypeptide chains. (23 refs.)

77-5116 **Lamella-Particle Complexes in Nuclei of Owl Monkey Kidney Cells Infected with *Herpesvirus saimiri*.** (Eng.) Banfield, W. G. (Lab. Pathology, NCI, NIH, Public Health Service, U.S. Dept. Health, Education, and Welfare, Bethesda, MD 20014); Lee, C. W.; Tralka, T. S.; Rabson, A. S. *J Natl Cancer Inst* 58(5): 1421-1425; 1977.

Confluent monolayer cultures of primary owl monkey kidney cells were inoculated with *Herpesvirus saimiri*. Electron microscopy revealed a complex consisting of ribosomelike particles and a striated lamella occurring in stacked, tubular, and twisted ribbonlike configurations in the cell nuclei. Similar structures have been seen in some human leukemias and in lymphoma of the northern pike. (10 refs.)

77-5117 **Transformation of Lymphocytes by Herpesvirus Papio.** (Eng) Falk, L. A. (Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL); Henle, G.; Henle, W.; Deinhardt, F.; Schudel, A. *Int J Cancer* 20(2): 219-226; 1977.

An attempt was made to transform different Simian lymphocytes with herpesvirus papio (HVP), baboon lymphocytes with Epstein-Barr virus (EBV), and human lymphocytes with HVP. Transformation of cotton-topped (CT) or white-lipped (WL) marmoset lymphocytes and of baboon lymphocytes occurred following cocultivation with x-irradiated cells of HVP-carrying lymphoblastoid cell lines (LCL), but human or squirrel monkey cells did not transform under these conditions. There was a striking difference between HVP-transformed CT and WL marmoset LCL with respect to expression of viral capsid antigen (VCA) and/or early antigen (EA): 5/9 CT cultures were positive, but 0/12 WL cultures. This may reflect a species difference in susceptibility. Both cultures failed to react with antibodies to EBV-specified nuclear antigen (EBNA). Baboon LCL were EBNA-negative, although some were VCA-positive and/or EA-positive. DNA-complementary RNA (cRNA) filter hybridization with EBV cRNA showed that transformed CT or WL marmoset cells contained at least 1-2 virus genome equivalents per cell, baboon cells 15-25 virus genome equivalents per cell. In conclusion, the presence of antibodies in the sera of old-world primates that cross react with VCA specified by EBV or HVP, but lack antibodies reacting to EBNA, implies that these primates carry their own EBV-like viruses. (24 refs.)

77-5118 **Structural and Biochemical Analysis of Viruslike Particles Present in Guinea Pigs with L_2C Leukemia.** (Eng) Dahlberg, J. E. (Lab. Tumor Virus Genetics, NCI, NIH, Bethesda, MD 20014); Perk, K.; Michalides, R. *Fed Proc* 36(9): 2290-2296; 1977.

The morphology of the viruslike particles originating in the tumor cells of L_2C leukemia and of the endogenous B-type RNA tumor virus of the guinea pig (GP virus) was compared. In addition, two sublines of L_2C leukemia were compared with respect to expression of these two classes of viruslike particles. In subline L_2C-1 leukemia, extracellular particles were present in the plasma that were indistinguishable from tissue culture-grown GP virus. The cation and substrate preferences of the plasma reverse transcriptase were similar to those of GP virus, in addition, 5% of the RNA in L_2C-1 plasma was homologous with GP virus RNA. In the L_2C-2 subline, however, no evidence of the GP virus, as measured by reverse transcriptase, was found. In both sublines, intracisternal A particles (possibly analogous to the murine intracisternal A particle) were found along with their associated extracellular particles, but no morphological evidence of their maturation and release (eg, by budding) was observed. A possible mode of release for the intracisternal particles is necrobiotic destruction of the cells; the extent of tumor cell destruction parallels the level of extracellular particles. Inoculation of normal or immunosuppressed newborn strain 2 guinea pigs, as well as a wide variety of cell lines of several species, with materials known to contain both GP virus and intracisternally derived viruslike particles gave no evidence of infection or neoplasia. (33 refs.)

77-5119 **Biochemical Properties of the B-Type Retravirus of Guinea Pigs and an Agent in the Plasma of Guinea Pigs with L_2C Leukemia.** (Eng) Schlom, J. (NCI, NIH, Bethesda, MD 20014); Michalides, R.; Perk, K.; Pearson, J.; Dahlberg, J. *Fed Proc* 36(9): 2310-2315; 1977.

The biochemical and physical properties of the B-type retravirus of guinea pigs induced by bromodeoxyuridine (BUdR) were compared with those of virus particles isolated from the plasma of guinea pigs with L_2C leukemia. Plasma particles and the retravirus had a similar density under comparable conditions. The DNA polymerase activity associated with the plasma particles had the same template and cation preferences as the retravirus reverse transcriptase. Extensive sequence homology between the leukemic plasma particle RNA and the BUdR-induced retravirus RNA, as determined by competitive molecular hybridization, suggested that these particles are similar or identical to the guinea pig retravirus. High levels of similar particles were isolated from the plasma of strain 2 guinea pigs that had been previously inoculated sc with L_2C leukemia cells. (33 refs.)

77-5120 **Endogenous Guinea Pig Retravirus and L_2C Leukemia.** (Eng) Nayak, D. P. (Dept. Microbiology and Immunology, Univ. California Sch. Medicine, Los Angeles, CA 90024); Davis, A. R. *Fed Proc* 36(9): 2305-2309; 1977.

5-Bromodeoxyuridine (BUdR)-induced guinea pig retraviral genes are expressed in leukemic L_2C guinea pig cells, but not in normal (nonleukemic) cells. Retraviral particles from any guinea pig tissue or from leukemic or nonleukemic guinea pigs can be activated by BUdR. The results of DNA:RNA hybridization led to the conclusion that proviral genes are already present in all guinea pig cells (normal, leukemic, or BUdR-treated). Crt_{112} analysis utilizing guinea pig retraviral complementary DNA yielded values that correspond to approx 320 copies/cell of viral RNA in leukemic spleen, 800 copies/cell of viral RNA in leukemic lymphoblasts, and a minimum of 5,000-10,000 copies/cell of viral RNA in BUdR-induced cells. No viral RNA (<0.2 copy/cell) was detected in normal guinea pig liver or spleen. The complete guinea pig viral genome is expressed in L_2C leukemic lymphoblasts, and the same messenger RNA species found in BUdR-induced cells are also present in L_2C leukemic lymphoblasts. (26 refs.)

77-5121 **In Vitro Studies on L_2C Leukemia: Isolation of Guinea Pig Herpes Virus from Mink Cells after Cocultivation with Leukemic Cells.** (Eng) Rhim, J. S. (Microbiological Associates, Bethesda, MD 20016); Vernon, M. L.; Green, I. *Fed Proc* 36(9): 2328-2332; 1977.

Guinea pig herpesvirus (GPHV) was isolated from mink lung cells cocultivated with BZ-L*C leukemic cells. Electron microscopy of the virus revealed numerous extracellular enveloped particles and many intracellular nucleocapsids. The isolated GPHV produced an extensive cytopathogenic (CP) effect in guinea pig, Vero, mink, and cat cells, a moderate CP effect in rat and SIRC cells, but a weak CP effect in human tumor cells and mouse embryo cells. In addition, complement-fixing antigen for human herpes simplex virus type 1 was detected in cell suspensions prepared from GPHV-infected mink lung cells. The virus was neutralized by anti-rabbit serum against GPHV isolated by another researcher, but not by anti-guinea pig serum to guinea pig cytomegalovirus. (26 refs.)

77-5122 **Temperature-sensitive Mutants of Herpes Simplex Virus Differ in the Capacity to Establish Latent Infections in Mice.** (Eng.) Lofgren, K. W. (Reed Neurological Res. Center, UCLA Sch. Medicine, Los Angeles, CA 90024); Stevens, J. G.; Marsden, H. S.; Subak-Sharpe, J. H. *Virology* 76(1): 440-443; 1977.

Five temperature-sensitive mutants of herpes simplex virus type 1 differed markedly in their ability to establish latent infections in the brains and spinal ganglia of outbred Swiss-Webster mice. Mutant "leakiness" is not the explanation for these results. (7 refs.)

77-5123 **Regulation of Herpesvirus Thymidine Kinase Activity in LM(TK-) Cells Transformed by Ultraviolet Light-irradiated Herpes Simplex Virus.** (Eng) Kit, S. (Div. Biochemical Virology, Baylor Coll. Medicine, Houston, TX 77030); Dubbs, D. R. *Virology* 76(1): 331-340; 1977.

The regulation of herpesvirus thymidine kinase (TK) activity was studied in herpes virus simplex types 1 and 2 (HSV-1 and HSV-2)-transformed TK-deficient LM(TK-) cells. TK activity was stimulated 6-9 hr after the cells were infected with TK- mutants of HSV-1 (HSV-1 TK-), HSV-2 (HSV-2 TK-), or marmoset herpesvirus (MarHV TK-). Inhibitors of DNA synthesis did not prevent this stimulation, but RNA and protein synthesis inhibitors did. Neither equine herpesvirus nor TK- mutants of vaccina virus enhanced TK activity, showing that stimulation was specific. HSV-1 B2015, a mutant incapable of inducing TK in LM(TK-) cells at 37 C, stimulated HSV-transformed cells at this temperature, suggesting that the TK gene probably functions normally in mutant B2105. These experiments suggest that TK enhancement by TK- HSV occurs independently of the superinfecting HSV's ability to produce an inactive TK polypeptide. Other autoradiographic and enzyme studies revealed TK activity in most HSV-1-transformed LM(TK-) cells grown in nonselective media. This activity was further enhanced by HSV-1 TK- infection, supporting the idea that the HSV TK gene was retained in most transformed cells grown in nonselective media. Anti-HSV-1 IgG and anti-HSV-2 IgG inhibited TK enhancement in HSV-1- and HSV-2-transformed LM(TK-) cells, even when the latter were superinfected with HSV-1 TK-, HSV-2 TK-, or MarHV TK-. Neither antiserum inhibited TK induction by wild-type MarHV in LM(TK-) cells, indicating that TK stimulation by TK- HSV infections of HSV-transformed cells had the antigenic specificity of the resident virus TK. (25 refs.)

77-5124 **New Data on Etiological Role of Herpesvirus in Tumorigenesis.** (Rus) Terekhina, N. A. (No affiliation given). *Patol Fiziol Eksp Ter* (3): 90-91; 1977.

The role of herpesvirus in the etiology of malignant tumors is discussed. Antibodies to herpes simplex virus type 2 (HSV-2) (genital type) were more frequent in patients with carcinoma of the cervix uteri than in healthy women; HSV-2 antigen was detected in cells exfoliated from the cervix uteri of women with preinvasive lesions. (20 refs.)

77-5125 **The Multiplication of Herpes Simplex Virus Type 2 (HSV-2) in Isolated Human Lymphocytes.** (Eng) Dostal, V. (Inst. Cancer Res., Univ. Vienna, Borschkegasse 8a, 1090 Vienna IX, Austria); Reiss-Gutfreund, R. J.; Binder, M. *Oncology* 34(5): 198-200; 1977.

Human lymphocytes that had been stimulated with phytohemagglutinin for 48 hr were infected with herpes simplex virus type 2 (HSV-2) at 0.5 TCID/ml. ^{3}H-Thymidine incorporation rates were markedly reduced at 7 and 29 hr postinfection. Electron microscopy of those cells at 25 hr showed the presence of naked nucleocapsids inside the nuclei and protein-coated nucleocapsids in the cytoplasm. The importance of HSV-2 multiplication in human lymphocytes in connection with chronically recurring infections is discussed briefly. (17 refs.)

77-5126 **Autoradiographic Detection of the Epstein-Barr Virus (EBV)-associated Early Antigen (EA) in Lymphoblastoid Cell Lines.** (Eng) Moar, M. H. (Dept. Tumor Biology, Karolinska Inst. Stockholm, Sweden); Siegert, W.; Klein, G. *Haematol Blood Transfus* 20: 283-287; 1977.

A sensitive method for the detection of Epstein-Barr virus (EBV)-associated antigens in lymphoblastoid cell lines is presented. Use of ^{125}I-labeled IgG directed against EBV early antigen (EA) or virus capsid antigen (VCA) followed by autoradiography resulted in the detection of EA and VCA in EBV-infected cell cultures. This method appeared to be more specific and more sensitive than direct or indirect immunofluorescence. (9 refs.)

77-5127 **Human Lymphoblastoid Cell Lines Derived from Individuals Without Lymphoproliferative Disease Contain the Same Latent Forms of Epstein-Barr Virus DNA as Those Found in Tumor Cells.** (Eng) Kaschka-Dierich, C. (Hygiene Institut, Universitat, Gottingen, W. Germany); Falk, L.; Bjursell, G.; Adams, A.; Lindahl, T. *Int J Cancer* 20(2): 173-180; 1977.

The physical charateristics of Epstein-Barr virus (EBV) DNA were studied in four lymphoblastoid cell lines (F-265, NC-37, U-303L, and PG-1) derived from individuals without lymphoproliferative disease and compared with two Burkitt's lymphoma lines, Raji and Rael. All six cell lines contained multiple copies of covalently closed, circular EBV DNA molecules of the same size, in addition to viral DNA with the properties of integrated DNA. No differences could be detected between the EBV DNA in the lymphoma cells and that in the lymphoblastoid cells from healthy individuals. (27 refs.)

77-5128 **Transcription of Latent Epstein-Barr Virus Genomes in Human Epithelial/ Burkitt Hybrid Cells.** (Eng) Tanaka, A. (Dept. Microbiology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612); Nonoyama, M.; Glaser, R. *Virology* 82(1): 63-68; 1977.

The level of transcription of the Epstein-Barr virus (EBV) genome was examined in three cell lines (D98/HR-1, D98/Raji, and Raji) in which there are different degrees of virus expression after induction with iododeoxyuridine (IUdR). All three cell lines contained viral RNA transcribed from approx 25% of viral DNA. IUdR treatment (60 μg/ml culture) of the three cell lines for 3 days induced transcription of 50% of the virus DNA. Raji cells, however, produced only early antigen (EA), whereas D98/HR-1 and D98/Raji produced EA and virus capsid antigens. This suggests that there may be some posttranscriptional control in Raji cells after IUdR induction. According to DNA-RNA hybridization kinetics, the amount of viral RNA in the cells was proportional to the number of viral genomes per cell, indicating that a constant fraction of the multiple copies of viral DNA is transcribed in the three cell lines. (13 refs.)

77-5129 **Productive Epstein-Barr Viral Infection of the Human Lymphoblastoid Cell Line 6410 with Release of Early Antigen Inducing and Transforming Virus.** (Eng) Traul, K. A. (Pfizer Incorporated, Maywood, NJ 07607); Stephens, R.; Gerber, P.; Peterson, W. D. *Int J Cancer* 20(2): 247-255; 1977.

The biological activity of a progeny strain of Epstein-Barr virus (EBV) was compared to the infecting, or parent, strain, P3HR-1-derived EBV. Subsequent to the first cycle of infection of human lymphoblastoid cell line 6410, characterized by early antigen (EA) and virus capsid antigen (VCA) synthesis, the culture, designated 6410-EBV, continued synthesizing VCA. Electron microscopy showed that the cells were productively infected with EBV. The virus, which was recovered from culture supernates, had the ability to induce EA synthesis in Raji cells and to transform human umbilical cord blood lymphocytes, in contrast to the P3HR-1 virus, which only induced EA. Histocompatibility antigen typing and karyotype analysis of P3HR-1, 6410, and 6410-EBV cultures indicated a relatedness of 6410-EBV to 6410 cells and a dissimilarity to P3HR-1. At present, only speculations can be offered for the differences in biologic activity between the parent P3HR-1 virus and the progeny virus. Perhaps the endogenous EBV genome of 6410 cells was activated and gave rise to a different strain of EBV or to a mixed progeny-parent strain as a result of dual infection, or the parent strain may have been modified as a result of interaction with the new host cell. (22 refs.)

77-5130 **Histochemical Studies on the EBV-determined Nuclear Antigen (EBNA).** (Eng) Ohno, S. (Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm 60, Sweden); Wiener, F.; Klein, G. *Biomedicine* 26(4): 268-275; 1977.

Histochemical studies of Epstein-Barr virus (EBV)-determined nuclear antigen (EBNA) revealed it to be a protein. Trypsin treatment destroyed EBNA staining, but treatments with RNAse, DNAse, and hyaluronidase did not. Prolonged treatment of EBNA-positive cells with DNAse was capable of decreasing chromosome-associated EBNA fluoresence, but not abolishing it entirely. Experiments showed that the DNAse acted by removing the binding sites (DNA) for EBNA, rather than by destroying EBNA. The effect of different fixatives on the antigenic activity of EBNA in Raji cells was examined. Methanol and acetone preserved EBNA staining well, but formaldehyde completely destroyed it. Moderated heat treatment (56 C) of fixed cells for periods up to 30 min gradually weakened EBNA positivity but 50% of the cells still remained positive. Treatment at 100 C for 10 sec, however, destroyed the EBNA reaction. Also, EBNA staining was sensitive to periodate, which suggests that carbohydrate groups are present. (26 refs.)

77-5131 **Heterogeneity of Epstein-Barr Virus. II. Induction of Early Antigens (EA) by Complementation.** (Eng) zur Hausen, H. (Institut fur Virologie, Zentrum fur Hygiene, Universitat Freiburg, Hermann-Herder-Strasse 11, 78 Freiburg, W. Germany); Fresen, K. O. *Virology* 81(1): 138-143; 1977.

The induction of early antigen (EA) following infection of B lymphoblasts was studied. Epstein-Barr virus (EBV) genomes were introduced into BJA EBV-negative human B lymphoma cells and into Ramos cells using viral isolates from P3HR-1 and B 95-8 cells. Cloned P3HR-1 virus-converted BJA cells contained two different Epstein-Barr nuclear antigen (EBNA) patterns. In a second experiment, parental BJA and Ramos lines, converted lines, BJA-HR1K clones, an EBNA-negative subclone (B1-28), and Raji cells were each infected with P3HR-1 or B 95-8 EBV. P3HR-1 virus-enhanced EA induction was 14 times greater in EBV genome-bearing cells than in genome-negative lines. B 95-8 virus-induced EA's were seen mainly in P3HR-1 virus-converted cells and, to a smaller extent, in Raji cells. EA induction in infected EBV genome-carrying cells was directly proportional to the concentration of infecting virus particles. In EBV genome-free cells, EA induction was reduced by the square of the dilution factor. These results suggest that resident genomes complement superinfecting genomes in EA induction by EBV and that two different populations of genomes are required for EA induction in infected B lymphoblasts. (12 refs.)

77-5132 **The Group C Adenovirus Tumor Antigens: Identification in Infected and Transformed Cells and a Peptide Map Analysis.** (Eng) Levinson, A. D. (Dept. Biochemical Sciences, Princeton Univ., Princeton, NJ 08540); Levine, A. J. *Cell* 11(4): 871-879; 1977.

Group C adenovirus (CAV) tumor antigens were studied via immunoprecipitation techniques and peptide map analysis. Serum from hamsters bearing CAV-induced tumors was divided into two classes: a broad-spectrum serum containing antibodies to the 72,000 (72K)-, 58K-, 44K-, and 17K-dalton early CAV proteins; and a narrow-spectrum serum precipitating only the 58K-dalton protein from virus-infected cell abstracts. Both types of serum specifically reacted with the 58K protein from type 2 adenovirus-transformed hamster cells and from type 2 adenovirus-SV40 nondefective hybrid (AD2+ND-1)-transformed hamster cells. The broad-spectrum serum precipitated a late 120K protein from virus-infected but not from virus-transformed cells. Peptide maps, on the other hand, indicated a close relationship between the 120K antigen and the 120K virus hexon structural protein. The 72K antigen (the adenovirus single-strand-specific DNA binding protein) contained all the peptides found in the 44K antigen plus two additional fragments. The 44K antigen is thus a likely proteolytic degradation product of the 72K protein. The peptide map of the 58K antigen was completely distinct from those of the other proteins. The 58K antigen thus appears to be antigenically unrelated to any previously described CAV gene product and may be the antigen common to all adenovirus-transformed cells. (32 refs.)

77-5133 **The Definition of a Large Viral Transcription Unit Late in Ad2 Infection of HeLa Cells: Map-**

ping by Effects of Ultraviolet Irradiation. (Eng.) Goldberg, S. (Rockefeller Univ., New York, NY 10021); Weber, J.; Darnell, J. E. *Cell* 10(4): 617-621; 1977.

UV irradiation of the nucleus of HeLa cells infected with adenovirus type 2 (AD2) resulted in decreased synthesis of RNA homologous to various DNA fragments from map positions 0.2-0.3 to 1.0. These results imply that transcription of AD2-DNA late in infection begins on the rightward-reading strand between 0.0 and 0.3; few, if any, promoters for late transcription exist to the right of this region. (17 refs.)

77-5134 **Two "Early" mRNA Species in Adenovirus Type 2-transformed Rat Cells.** (Eng.) Flint, S. J. (Dept. Biochemical Sciences, Princeton Univ., Princeton, NJ 08540). *J Virol* 23(1): 44-52; 1977.

The size distribution and genome localization of viral messenger RNA (mRNA) species synthesized during the early phase of productive adenovirus 2 (Ad2) infection and in two lines of Ad2-transformed rat embryo cells were examined. The mRNA was fractionated on sucrose gradients after disaggregation. Viral mRNA species were identified by hybridization across these gradients with the separated strands of restriction endonuclease fragments of ^{32}P-labeled DNA known to be complementary to Ad2 early and Ad2-transformed cell mRNA. mRNA transcribed from the left-hand 14% of the Ad2 genome comprised two species, 16S-17S and 20S-22S: the same-sized mRNA's were present both at early times during productive infection and in the two transformed rat cell lines. Direct comparison of the sequences present in these two mRNA species by additional saturation hybridizations suggests that they are not related to one another. Three additional regions of the Ad2 genome, all of which are located in the right-hand 40% of the genome, are complementary to early mRNA sequences and each appears to specify one major mRNA species of 22S. Taking the sizes of the 22S, 20S-21S, and 16S-17S viral mRNA species, estimated from their sedimentation behavior and from saturation hybridization experiments as upper and lower limits, respectively, of their coding capacities, it is estimated that these three species encode 59,000-78,000, 50,000-65,000, and 35,000-48,000 daltons of protein, respectively. It is unnecessary to postulate the existence of different transcriptional modes of Ad DNA sequences present in the various environments of productively infected and transformed cells. (43 refs.)

77-5135 **Structure of the Inverted Terminal Repetition of Adenovirus Type 2 DNA.** (Eng.) Wu, M. (Dept. Chemistry, California Inst. Technology, Pasadena, CA 91125); Roberts, R. J.; Davidson, N. *J Virology* 21(2): 766-777; 1977.

The duplex projection from the single strand circle of adenovirus 2 DNA due to the terminal inverted repeat was positively identified. Its length was estimated at 125 nucleotide pairs by both the low formamide-cytochrome *c* spreading and the gene 32-ethidium bromide techniques. (22 refs.)

77-5136 **In Vitro Traits of Adenovirus-Transformed Cell Lines and Their Relevance to Tumorigenicity in Nude Mice.** (Eng.) Gallimore, P. H. (Dept. Cancer Studies, Univ. Birmingham, The Medical Sch., Birmingham B15 2TJ, England); McDougall, J. K.; Chen, L. B. *Cell* 10(4): 669-678; 1977.

In vitro traits (serum requirements, saturation density, anchorage independence, proteolytic enzyme activity, and the presence of LETS glycoprotein and T antigen) and their importance for the in vivo growth potential of six adenovirus 2 transformed rat embryo cell lines and one adenovirus 5 transformed human cell line were assessed; reduced levels of LETS protein was the only correlate to malignancy. This series of cell lines exhibited an oncogenic spectrum ranging from tumorigenicity in immunocompetent rats to lack of tumorigenicity in nude mice. (23 refs.)

77-5137 **Evidence for a Function of the Adenovirus DNA-binding Protein in Initiation of DNA Synthesis as well as in Elongation of Nascent DNA Chains.** (Eng.) van der Vliet, P. C. (Lab. Physiological Chemistry, State Univ. Utrecht, Vondellaan 24 A, Utrecht, Netherlands); Zandberg, J.; Jansz, H. S. *Virology* 80(1): 98-110; 1977.

Early in the infection of human or monkey cells with adenovirus type 5 (Ad5), a single-strand-specific DNA binding protein with a molecular wt of 72,000 is produced. Two different inactivation methods were used to study the function of this protein in viral DNA synthesis. When KB cells infected with the early temperature-sensitive (ts) mutant H5ts125 were grown at the permissive temperature (32 C) followed by a shift to the nonpermissive temperature (40 C), viral DNA synthesis was reduced at least tenfold within 1 hr. The start of the first and subsequent rounds of DNA replication was inhibited. Viral DNA synthesis in H5ts125-infected KB nuclei, however, was not thermosensitive. Replicating H5ts125-DNA molecules were converted to mature DNA in isolated nuclei without reinitiation of new replication rounds. These results show that thermal inactivation of the H5ts125 DNA-binding protein destroys its capacity to function in the initiation of new replication rounds but does not impair chain growth. Viral DNA synthesis in vitro was also studied in the presence of antibody against the purified DNA-binding protein. There was an inhibition of the viral DNA synthesis rate, but cellular DNA synthesis was not affected. Density-labeling experiments showed that the antibody inhibits the duplication of both complementary strands, by decreasing fork movement in replicating Ad DNA. The results suggest that the Ad5 DNA-binding protein functions in the initiation of DNA replication as well as in the elongation of nascent viral DNA chains. (26 refs.)

77-5138 **Characteristics of a Human Cell Line Transformed by DNA from Human Adenovirus Type 5.** (Eng.) Graham, F. L. (Dept. Biology, McMaster Univ., Hamilton, Ontario, Canada); Smiley, J.; Russell, W. C.; Nairn, R. *J Gen Virol* 36(1): 59-72; 1977.

Sheared fragments of adenovirus type 5 (strain Ad75) DNA were used to transform human embryonic kidney cells (HEK). Of eight transformation experiments (20 cultures of HEK cells/experiment), only two were successful. In each a single morphologically transformed colony was observed approximately 1 mo after exposure. The transformed cells displayed many of the characteristics of transformation, including elaboration of a virus-specific tumor antigen. There was a variable pattern of polypeptide synthesis in the cells that differed in several respects from that seen in other human cells. Upon labeling the cell surface by lactoperoxidase-catalyzed radioiodination, the absence of a labeled polypeptide similar to the 250,000 (LETS, large external transformation-sensitive) glycoprotein was noted. Hybridization of labeled cellular RNA with restriction fragments of Ad5 DNA indicated transcription of a portion of the adenovirus genome at the left end. The tumor-inducing ability of the cells was tested by inoculating 5- to 6-wk-old nude mice with 1 to 2 $\times 10^7$ cells sc. Since no tumors appeared by 6-8 wk, the mice were reinoculated. Tumors appeared in 3/20 mice 15-20 wk after the first injection. Rat or hamster cells transformed by Ad5 DNA produced tumors in 90%-100% of mice in 3-6 wk. (30 refs.)

77-5139 **Deoxyribonuclease Activity Associated with Adenovirus 5 and 7.** (Eng.) Cajean-Feroldi, C. (Institut de Recherches Scientifiques sur le Cancer, Boite postale 8, F-948000 Villejuif, France); Chardonnet, Y.; Chantepie-Auray, J. *Eur J Biochem* 74(3): 457-462; 1977.

Adenoviruses 5 and 7 showed a max DNase activity with cellular DNA as substrate at a pH of 5.5 and 7.0 for adenovirus 5 and only at pH 7.0 for adenovirus 7. Both DNases were found in the penton fraction. No DNase activity was detectable in purified virions. (26 refs.)

77-5140 **Viral DNA Sequences from Incomplete Particles of Human Adenovirus Type 7.** (Eng) Tibbetts, C. (Dept. Microbiology, Sch. Medicine, Univ. Connecticut Health Center, Farmington, CT 06032). *Cell* 12(1): 242-249; 1977.

Large pools of empty viral capsids accumulate in cells infected with subgroup B human adenoviruses. The infected cells also yield DNA-containing incomplete particles in larger quantities than cells infected with serotypes representing other adenovirus subgroups. The DNA isolated from purified classes of adenovirus 7 (Ad7) incomplete particles was analyzed by restriction endonuclease cleavage, gel electrophoresis, and electron microscopy. At least 90% of the DNA molecules in each sample consisted of sequences that extended from the left end of the viral genome map by variable lengths toward the right end. The av length of the DNA was linearly related to the av buoyant density of the incomplete particles from which the DNA was isolated. Each capsid contained one DNA molecule. There was also a specific association of the left end of the viral genome with assembled or assembling capsids. The characteristic distributions of Ad7 incomplete particles may result from intracellular pools of assembly intermediates in which the incompletely packaged DNA has been fragmented in vivo or by shear during preparative procedures. (22 refs.)

77-5141 **The Relationship Between the Formation of Inclusions and Viral DNA Synthesis in Adenovirus 12-infected Cells.** (Eng.) Yamaguchi, K. (Dept. Pathology, Inst. Medical Science, Univ. Tokyo, Post Office Takanawa, Tokyo, 108, Japan); Shiroki, K.; Shimojo, H. *Virology* 80(1): 136-148; 1977.

The relationship between the formation of inclusions and viral DNA synthesis was investigated in cells infected with three human adenovirus 12 (H12), DNA-minus, temperature-sensitive (*ts*) mutants (*ts*A, *ts*B, and *ts*C) and with H12 wild-type (WT) virus in the presence of inhibitors of DNA synthesis. The three mutants are defective in DNA synthesis at the restrictive temperature (40 C). Inclusions were either absent or abortively formed in cells infected with the *ts* mutants at 40 C, although inclusions comparable to those in WR-infected cells were observed in cells infected at the permissive temperature (34 C). Inclusions formed at 34 C in *ts* A-infected cells disintegrated after temperature shift-up, in parallel with the cessation of DNA synthesis. In contrast, inclusions formed at 34 C in *ts*B- or *ts*C-infected cells were preserved at 40 C, although DNA synthesis was reduced markedly. This suggests that the morphological integrity of the inclusions depends on gene A, and their function on genes A, B, and C. Temperature shift-down of *ts*A-infected cells also showed the formation of inclusions and recovery in DNA synthesis. Inclusions were not formed in WR-infected cells when DNA synthesis was inhibited with cytosine arabinoside (ara-C) or hydroxyurea (HU). DNA synthesis was not induced and inclusions were not formed upon removal of ara-C, but the reverse was true for HU. Type II inclusions, but not type IV inclusions or virions, were formed in H12-infected monkey cells, suggesting that type II inclusions are involved in viral DNA synthesis, type IV inclusions in the accumulation of late proteins and virion assembly. (18 refs.)

77-5142 **Retinoblastoma-like Neoplasm Induced in C3H/BifB/Ki Strain Mice by Human Adenovirus Serotype 12.** (Eng) Mukai, N. (Wesley C. Bowers Lab. Pharmacology and Experimental Pathology, Eye Res. Inst., Retina Foundation, Boston, MA 02114); Nakajima, T.; Freddo, T.; Jacobson, M.; Dunn, M. *Acta Neuropathol (Berl)* 39(2): 147-155; 1977.

Within 24 hr of birth, 80 C3H/BifB/Ki mice received a single intraocular inoculation of 0.002-0.003 ml of human adenovirus 12 (Ad12). Of the 40 mice that survived, 7 developed a solid retinoblastomalike neoplasm between 64 and 236 days postinoculation. The tumors were successfully cultured and also transplanted sc into syngeneic hosts. Morphologically, all the tumors had the characteristic features of retinoblastoma associated with Homer Wright rosettes. Bizarre giant cells were detected frequently. AD12-specific T antigens were demonstrated in the primary and cultured tumor cells by immunofluorescent techniques. Some giant cells had numerous T-positive filaments. Electron microscopy showed poorly differentiated unipolar cells with a large ovoid nucleus. Many cells contained a well-organized solitary cilium consisting of a typical ring of nine doublets with no axial pair (9 + 0) in close association with a pair of centrioles. Some multinucleated giant tumor cells also contained multiple cilia-centriole complexes within their broad syncytial cytoplasm. Endogenous C-type viruslike particles were present in the retinal tumors, and they were indistinguishable from those found in murine neuroblastomas. The occurrence of tumors in mice of a pure strain adds to the range of known animals sensitive to Ad12 oncogenesis. (29 refs.)

77-5143 **Multiple Copies of Human Adenovirus 12 Genomes Are Integrated in Virus-induced Hamster Tumors.** (Eng.) Green, M. R. (Inst. Molecular Virology, Saint Louis Univ. Sch. Medicine, St. Louis, MO 63110); Mackey, J. K.; Green, M. *J Virol* 22(1): 238-242; 1977.

Tumors induced in newborn hamsters by highly oncogenic adenovirus 12 contained multiple copies of 90-100% of the viral genome in an integrated state. (17 refs.)

77-5144 **The Dynamics of the Isoenzyme Spectrum of Some Energy Metabolism Enzymes and the Ultrastructures of Mitochondria in Viral Carcinogenesis.** (Rus) Ageenko, A. I. (Lab. Virology, P. A. Gertsen Res. Inst. Oncology, Moscow, USSR); Iagubov, A. S.; Vitorgan, Iu, E.; Kats, V. A. *Biull Eksp Biol Med* 34(8): 205-208; 1977.

The isoenzyme spectrum of lactate dehydrogenase and malate dehydrogenase human adenovirus 12-infected rat embryo fibroblasts was determined and compared to controls. Spectral shifts of the two enzymes were noted in both the nuclei and the cytoplasm on the first few days of culture and were not related to cell proliferation. A comparison of mitochondrial fine structure with the kinetics of these shifts indicated that the enzymatic changes occurred almost from the moment of infection. (15 refs.)

77-5145 **Preparation and Characterization of Highly Radioactive In Vitro Labeled Adenovirus DNA and DNA Restriction Fragments.** (Eng) Mackey, J. K. (Inst. for Molecular Virology, Saint Louis Univ. Sch. Medicine, Saint Louis, MO 63110); Brackmann, K. H.; Green, M. R.; Green, M. *Biochemistry* 16(20): 4478-4483; 1977.

A simple microscale procedure is described for the synthesis and purification of high specific activity α-^{32}P-deoxyribonucleoside 5′ triphosphates [300-1,300 Ci/millimoles (mmol)] which can be used to label as little as 56 nanograms of adenovirus DNA or DNA restriction fragments to specific activities up to 4 x 10^8 cpm/μg by in vitro repair synthesis (nick translation). ^{3}H-DNA of specific activity 1.5 x 10^7 cpm/μg was also prepared by nick translation using commercial ^{3}H-thymidine 5′ triphosphate (50 Ci/mmol). The products were extensively characterized as to reassociation properties. Adenovirus 12 DNA and the *Eco*RI restriction fragments labeled by this procedure were identical with in vivo labeled viral DNA according to the following three types of molecular hybridization measurements: copy number determination, by reassociation kinetics, of viral DNA in viral transformed cells; renaturation rate of viral DNA and restriction fragments and agreement with genetic complexity; and saturation-hybridization of labeled viral DNA with unlabeled restriction fragments. The distribution of radioactivity in restriction fragments prepared from in vitro labeled DNA showed that viral DNA was uniformly labeled in vitro. These studies demonstrated that this in vitro labeling procedure produces sensitive, accurate, and representative DNA probes and provides an economical and versatile method for detecting homologous nucleic acid sequences in small quantities of viral, cellular, or tissue nucleic acids. (34 refs.)

77-5146 **Molecular Similarities Among the Adenovirus-associated Virus Polypeptides and Evidence for a Precursor Protein.** (Eng.) Johnson, F. B. (Dept. Microbiology, Brigham Young Univ., Provo, UT 84602); Thomson, T. A.; Taylor, P. A.; Vlazny, D. A. *Virology* 82(1): 1-13; 1977.

The structural polypeptides (VP1, VP2, and VP3) of adenovirus-associated virus (AAV) were similar in their content of leucine, lysine, and aspartic acid. They also demonstrated high levels of antigenic similarity and unique regions of antigenic nonhomology. Several nonstructural polypeptides were found in infected cells, one of which (VP0) has a kinetic relationship with VP1, VP2, and VP3 and could be the primary AAV gene product processed to these proteins and to other, nonstructural fragments during the AAV replicative cycle. (23 refs.)

77-5147 **A Transforming Cytomegalovirus from the Human Prostate (Meeting Abstract).** (Eng) Webber, M. M. (Div. Urology, Univ. Colorado Medical Center, Denver, CO 80262); Rapp, F. *In Vitro* 13(3): 160-161; 1977. (no refs.)

77-5148 **RNA-Reverse Transcriptase Complex from Cultured Human Myeloma-Leukemia Cells.** (Eng) Sawada, H. (Dept. Internal Medicine, Faculty Medicine, Kyoto Univ. Sakyo-Ku, Kyoto 606, Japan); Tashima, M.; Nakamura, T.; Uchiyama, T.; Sagawa, K.; Takatsuki, K.; Uchino, H.; Ito, Y. *Int J Cancer* 20(1): 15-20; 1977.

Media from cultures of peripheral WBC obtained from two patients with myeloma-leukemia contained high-mol-wt RNA-reverse transcriptase complexes. Both components banded at about 1.16-1.18 g/ml in isopycnic sucrose gradients sedimentations, a density typical of oncornaviruses. The RNA showed two peaks, at approx 50S and 23S, in velocity sedimentation analysis. The DNA polymerase activity could utilize poly(rA)·oligo dT and poly(rC)·oligo dG as template primer, but not poly(dA)·oligo dT or oligo dT, suggesting reverse transcriptase activity. The possibility of oncornaviruses as etiological agents in human multiple myeloma was considered. (20 refs.)

77-5149 **Study of the Specificity of Leukocyte Virus of Human Leukemia.** (Rus) Barinskii, I. F. (D. I. Ivanovskii Inst. Virology, USSR Acad. Medical Sciences, Moscow, USSR); Shubladze, A. K.; Ugriumov, E. P.; Tsypkin, I. S.; Bocharov, A. F.; Posevaia, T. A.; Dadashev, Kh. Iu.; Zaitseva, A. I. *Vopr Virusol* (2): 164-168; 1977.

The antigen of WBC leukemia virus (WLV) was detected in the cytoplasm of cells from 19/32 bone marrow punctures and in the WBC from 10/12 blood smears of patients with acute leukemias and chronic myelocytic leukemia. The antibody-infected cells were found in 60.8% of the leukemia patients as compared to only 18.5% of controls. Gel precipitation revealed that the WLV antigen contained neither a group-specific antigen of murine leukemia virus nor oncornavirus D antigen from the HEp-2 continuous cell line. (12 refs.)

77-5150 **Virus-like Particles in Placentas from Normal Individuals and Patients with Systemic Lupus Erythematosus.** (Eng) Dirksen, E. R. (Dept. Anatomy, Sch. Medicine, Univ. California, Los Angeles CA 90024); Levy, J. A. *J Natl Cancer Inst* 59(4): 1187-1192; 1977.

Nineteen placentas, 9 from normal women and 10 from women with systemic lupus erythematosus (SLE), were examined by electron microscopy. Virus-like particles were found in four of the normal women (44%) and in three of the women with SLE (30%). There was no difference in the frequency of the virus in any of these patients; in all cases they were found in the basal infoldings of the syncytiotrophoblast cells of the chorionic villi. (12 refs.)

77-5151 **Reactivity of Antisera to Oncorna Virus Proteins with Human Leukemia Cells.** (Eng) Oliver, R. T. (Imperial Cancer Res. Fund, Dept. Medical Oncology, St. Bartholomew's Hosp., London EC1, England); Pillai, A. *Proc R Soc Med* 70(1): 556-559; 1977.

Cells from 28 leukemia patients with active untreated disease, 8 leukemia patients in complete remission and off all chemotherapy, and 8 normal persons were studied with antisera against Moloney leukemia virus proteins and simian sarcoma virus (SiSAV) proteins. There was more cytotoxicity and reactivity against the SiSAV proteins than the Moloney proteins for all three groups, but the leukemia cells were more reactive than the other two classes. These sera and three others against Moloney virus proteins, control normal rabbit sera and sera produced by immunizing rabbits with androstendione in Freund's adjuvant were used in further experiments. Acute lymphoblastic leukemia cells had the highest reactivity followed be acute myeloid leukemia (AML) and chronic lymphocytic leukemia. Control sera were usually negative although there were two weak reactions of 50% and 25% against AML cells with normal rabbit sera and a weak reaction with 1/11 normal human sera. It was too early to determine whether these findings were due to the presence of a viral protein on human leukemia cells. (13 refs.)

77-5152 **The Influence of Exogenous Interferon on the Course of Latent Oncornavirus Infection of J-**

96 Cells. (Rus) Solov'ev, V. D. (Central Inst. Postgraduate Medical Studies, Moscow, USSR); Kishchak, V. Ia.; Bektemirov, T. A.; Bocharov, A. F.; Moisiadi, S. A.; Delimbetova, G. A.; Chuev, Iu. V. *Vopr Virusol* (2): 196-202; 1977.

The effect of exogenous WBC interferon (10 units/ml) was investigated in chronic oncornavirus infection of lymphoblastoid J-96 cells producing type B virus. After 18 to 34 passages, virion formation was inhibited 2.0- to 4.4-fold and virus budding was inhibited 1.6- to 2.7-fold. There was no inhibiting effect on the formation of intracytoplasmic type A virions. The oncornavirus that was produced retained its biological activity in KC cells. Electrophoresis of the cell membranes showed an accumulation of 115,000, 100,000 and 68,000 mol wt glycoproteins in the cell fraction. The cells were also found to have two- to three-fold increases in the inter-species group-specific antigen of Mason-Pfizer virus. The mechanism of action of interferon is discussed. (20 refs.)

77-5153 **Characterization of Single Cell Clones Derived from Mason Pfizer Virus-transformed Rhesus Monkey Cell Cultures (Meeting Abstract).** (Eng) Brown, B. L. (NCI Frederick Cancer Research Center, P. O. Box B, Frederick, MD 21701); Fine, D. L.; Kmetz, J. P. *In Vitro* 13(3): 175; 1977. (no refs.)

77-5154 **A New Genetic Locus, *Bevi*, on Human Chromosome 6 Which Controls the Replication of Baboon Type C Virus in Human Cells.** (Eng) Lemons, R. S. (Lab. Viral Carcinogenesis, NCI, Bethesda, MD 20014); O'Brien, S. J.; Sherr, C. J. *Cell* 12(1): 251-262; 1977.

Somatic cell hybrids from seven independent fusions between mouse x human and hamster x human parental cells were examined for their ability to support the replication of baboon endogenous C-type virus. These hybrids preferentially segregated human chromosomes while retaining rodent chromosomes, as demonstrated by karyotype and isozyme analyses. A total of 41 primary colonies and 33 secondary sublcones were analzyed for viral replication and for the presence of enzyme structural gene markers for 19/23 human chromosomes. A syntenic association was seen between the ability of the baboon C-type virus to infect and replicate in hybrid cultures and the expression of human malic enzyme-1 (assigned to human chromosome 6). Analysis of 86 highly segregated subclones derived from cells preinfected with baboon C-type virus showed that continued virus production segregated concordantly with the expression of three enzyme genes assigned to human chromosome 6 (malic enzyme-1, phosphoglucomutase-3, and superoxide dismutase-2). Subclones of infected hybrids that lost chromosome 6 and failed to release virus also failed to synthesize the virus-coded major structural protein p30. No syntenic association between baboon virus expression and any of 18 other human chromosomes was observed. These studies define a new gene (designated *Bevi*) on human chromosome G that controls the replication of baboon C-type virus. The data suggest that *Bevi* may be a preferred integration site for the baboon C-type DNA provirus in the human genome. (53 refs.)

77-5155 **Infectious Primate Type-C Virus Shed by Healthy Gibbons.** (Eng.) Kawakami, T. G. (Comparative Oncology Lab., Univ. California, Davis, CA 95616); Sun, L.; McDowell, T. S. *Nature* 268(5619): 448-450; 1977.

Studies were performed to determine whether healthy captive gibbons (*Hylobates*) were a source of infectious primate type-C virus. Gibbons having long term asymptomatic type-C viremia without detectable immune responses actively shed infectious virus in their urine and feces. None of the normal or antibody-positive gibbons excreted infectious virus. (23 refs.)

77-5156 **Yaba Virus-specific DNA in the Host Cell Nucleus.** (Eng) Taylor, J. L. (Lab. Molecular and Cancer Virology, Dept. Microbiology, Southern Illinois Univ., Carbondale, IL 62901); Rouhandeh, H. *Biochim Biophys Acta* 478(1): 59-67; 1977.

Investigations were performed to determine whether Yaba virus DNA is present in infected Jinet and CV-1 cells and to characterize its nature. Hybridization of nuclear DNA with virus DNA indicated that a max of 1.1% of the infected nuclear DNA is homologous with the Yaba virus DNA. Yaba virus DNA was not covalently linked to the host cell DNA. In spite of a reduction in host DNA synthesis during infection, this synthesis was not totally stopped. Yaba virus DNA was synthesized in the nucleus, since the level of incorporation of label was 10 times the background level in the cytoplasm. Treatment of isolated nuclei with sodium dodecyl sufate and EDTA following precipitation with 1 M NaCl removed most of the cellular DNA from the viral DNA. (21 refs.)

77-5157 **SV-40 T Antigen Expression in Skin Fibroblasts from Normal Individuals, Patients with Fanconi's Anemia, and a Family at High Risk of Leukemia.** (Eng.) Lubiniecki, A. S. (Life Sciences Div. Meloy Labs., Inc., Springfield, VA 22151); Blattner, W. A.; Fraumeni, J. F. *In: Genetics of Human Cancer.* Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F. (New York: Raven Press): Progress in Cancer Research and Therapy 3: 377-381; 1977.

An improved standardized and reproducible transformation assay is described, which uses the expression of simian virus-40 T antigen detected by immunofluorescence as the end point only three days after infection. (18 refs.)

77-5158 **Purification of Simian Virus 40 Tumor Antigen from a Line of Simian Virus 40-Transformed Human Cells.** (Eng) Tenen, D. G. (Div. Medical Oncology, Sidney Farber Cancer Inst., Boston, MA 02115); Garewal, H.; Haines, L. L.; Hudson, J.; Woodard, V.; Light, S.; Livingston, D. M. *Proc Natl Acad Sci USA* 74(9): 3745-3749; 1977.

A method for the purification of Simian virus 40 (SV40) tumor (T) antigen is presented. SV80 cells were homogenized and the extract fractionated with ammonium sulfate. This pool was chromatographed on DEAE cellulose and the peaks containing the antigen fraction chromatographed on QAE-Sephadex and heparin-Sepharose. The appropriate fraction was then sedimented through a glycerol density gradient. The yield from this preparation was usually ≥ 3%. The mol wt of the antigen was estimated at 90,000 to 94,000. Amino acid analysis revealed that the protein is rich in glycine and serine. (39 refs.)

77-5159 **Purification of Simian Virus 40 and JC T-Antigens from Transformed Cells.** (Eng) Cikes, M. (Ludwig Inst. for Cancer Res. 1066 Epalinges-sur-Lausanne, Switzerland); Beth, E.; Guignard, N.; Walker, D. L.; Padgett, B. L.; Giraldo, G. *J Natl Cancer Inst* 59(3): 889-894; 1977.

A new technique for purifying simian virus 40 (SV40) and JC virus T antigens from transformed hamster cells is described. Crude lysates from SV40-transformed cells were chromatographed on a Biogel column under dissociating nondenaturing conditions. Immunoreactive material from the peak occurring between the elution volumes of bovine serum albumin and IgG was further purified by ion exchange chromatography on diethylaminoethylcellulose and phosphocellulose columns. The specific activity of the final product was increased 166-fold over that of the crude lysate, and the total recovery was 15.9%. A similar procedure was applied to JC T antigen from JC virus-transformed cells. Elution profiles from the latter purification were similar to those obtained with SV40 T antigen. However, JC T antigen proved even more labile than SV 40 antigen, resulting in a lower end-product specificity. (31 refs.)

77-5160 **Stimulation of RNA Synthesis in Isolated Nuclei by Partially Purified Preparations of Simian Virus 40 T-Antigen.** (Eng) Ide, T. (Dept. Pathology, Temple Univ. Health Sciences Center, Philadelphia, PA 19140); Whelly, S.; Baserga, R. *Proc Natl Acad Sci USA* 74(8): 3189-3192; 1977.

The effects of partially purified tumor (T)-antigen preparations on RNA synthesis in isolated nuclei was studied. T antigen was partially purified from nuclei of cells transformed by simian virus 40 (SV40). Nuclei isolated from either rat liver or quiescent AF8 hamster cells were preincubated with T-antigen preparations; there was a marked stimulation of RNA synthesis, up to 150% above controls. This stimulation was inhibited by hamster antiserum against T antigen but not by normal hamster serum. When the T-antigen preparations were fractionated on glycerol gradients, fractions containing complement-fixing activity with antiserum to T antigen also had the highest stimulatory activity on nuclear RNA synthesis. T antigen was also partially purified from the nuclei of cells transformed by a temperature-sensitive (ts) A mutant of SV40. When preincubated up to 2 hr at 50 C, the T-antigen preparation from these ts A mutants was rapidly inactivated, in terms of complement-fixing activity and ability to stimulate RNA synthesis in isolated rat liver nuclei. Under the same preincubation conditions, T antigen preparations from cells transformed by wild-type SV40 maintained their complement-fixing ability and their ability to stimulate RNA synthesis. These results suggest that T antigen stimulates cellular RNA synthesis, but final confirmation awaits its satisfactory purification. (42 refs.)

77-5161 **The Extensive Homology Between mRNA Sequences of Normal and SV40-transformed Human Fibroblasts.** (Eng) Williams, J. G. (Imperial Cancer Res. Fund, Mill Hill Lab., Burtonhole Lane, London NW7 1AD, England); Hoffman, R.; Penman, S. *Cell* 11(4): 901-907; 1977.

A high degree of homology was found between the poly(A)-containing messenger RNA (mRNA) of normal diploid MGF451 fibroblasts and simian virus 40 (SV40)-transformed progeny, as determined via cross-hybridization with labeled complementary DNA. Less than 3% of the sequences in mRNA from transformed cells were absent from the normal parental line. Many of the differences between the two lines occurred in RNA molecules of low and intermediate complexity. Extension homology in mRNA sequences from disparate cell lines may be a general phenomenon. Even HeLa cell mRNA is nearly identical to that of diploid human fibroblasts. (13 refs.)

77-5162 **Novel Mechanism for RNA Maturation: The Leader Sequences of Simian Virus 40 mRNA Are Not Transcribed Adjacent to the Coding Sequences.** (Eng) Aloni, Y. (Lab. DNA Tumor Viruses, NCI, NIH, Bethesda, MD 20014); Dhar, R.; Laub, O.; Horowitz, M.; Khoury, G. *Proc Natl Acad Sci USA* 74(9): 3686-3690; 1977.

The transcription of Simian virus 40 (SV40) messenger (m)RNA was studied in African green monkey kidney cells infected with 20 to 60 plaque forming units SV40/cell. The 16S and 19S cytoplasmic RNA fragments were isolated from poly(A) containing cytoplasmic RNA that mapped to DNA fragments between 0.67 and 0.76. They had previously been mapped between 0.95 and 0.17, and 0.77 and 0.17, respectively. Mapping of the 16S fragment revealed that the 5′-terminal sequences did not contain poly(A) directly adjacent to their 3′ termini. A map of the 5′ end of the fragment suggested that the region found to map between 0.95 and 0.17 is covalently linked to sequences transcribed between 0.67 and 0.76. These leader sequences contain the "cap" structure. A similar mechanism is proposed for the 19S RNA component. (14 refs.)

77-5163 **Nucleotide Sequence of the Gene for the Major Structural Protein of SV40 Virus.** (Eng) Pan, J. (Dept. Human Genetics, Yale Univ. Sch. Medicine, New Haven, CT 06510); Reddy, V. B.; Thimmappaya, B.; Weissman, S. M. *Nucleic Acids Res* 4(8): 2539-2548; 1977.

The gene coding for the major structural protein (VP1) of simian virus 40 (SV40) was sequenced. The gene contains 361 codons, and the appearance of synonym codons for given amino acids is not random. The dinucleotide CG occurs only once, and there is a 2:1 preference for uridylic acid in the third position of the codons. There are no readily apparent long repeats or other symmetry elements within the SV40 DNA sequence coding for VP1. (18 refs.)

77-5164 **Transcription of SV 40 Nucleoprotein Complexes In Vitro.** (Eng.) Cremisi, C. (Dept. Molecular Biology, Inst. Pasteur, 75015 Paris, France); Chestier, A.; Dauguet, C.; Yaniv, M. *Biochem Biophys Res Commun* 78(1): 74-82; 1977.

An attempt was made to clarify the fate of nucleosomes during gene expression of simian virus 40. In vitro studies of transcription of these complexes with *Escherichia coli* RNA polymerase suggested that the nucleosomes block the elongation of RNA in vitro. The process of viral genome transcription in vivo may require continuous nucleosome modifications comparable to the modified state of nucleosomes in active genes. (35 refs.)

77-5165 **Symmetric Transcription of Simian Virus 40 DNA in the Nuclei of Transformed Mouse Cells.** (Eng.) Yanagi, K. (Dept. Biochemistry, New York Univ. Sch. Medicine, 550 First Ave., New York, NY 10016); Zouzias, D.; Rush, M. G. *Biochem Biophys Res Commun* 78(1): 210-216; 1977.

RNA isolated from the cytoplasm of the simian virus 40 (SV40) transformed mouse 3T3 cell line, SV101, contained asymmetrically transcribed base sequences complementary to only the early region of the SV40 genome. In contrast, RNA isolated from purified nuclei contained symmetrically transcribed sequences complementary to all regions. These results indicate the involvement of selective processing and/or transport in the expression of viral information. (21 refs.)

77-5166 **The Nucleotide Sequence of Repetitive Monkey DNA Found in Defective Simian Virus 40.** (Eng) Rosenberg, M. (Lab. Molecular Biology, NCI, Bethesda, MD 20014); Segal, S.; Kuff, E. L.; Singer, M. F. *Cell* 11(4): 845-857; 1977.

The nucleotide sequence of the (Hind II/Hind III)-E fragment consisting of 151 base pairs (bp) and the first 33 bp of the (Hind II/Hind III)-C fragment from a defective Simian virus (SV) 40 genome isolated by restriction endonuclease cleavage were determined. RNA and DNA sequencing methods using the BSC-1 line of monkey kidney cells revealed that the 151 bp fragment may represent as much as 4.8% of the cell genome. This would correspond to a reiteration frequency of about 1.6×10^6 in the monkey genome. Digestion of total monkey DNA with endonuclease R.Hind III produced large amounts of DNA fragments containing regions homologous to the isolated fragment. The nucleotide sequences of 33 bp fragment that are contiguous to the 151 bp fragment were determined. Studies with other defective SV40 genomes indicated that sequences of the (Hind II/Hind III)-E fragment hybridized with fragments in the other defective viruses. Hybridization was only observed, however, with defective variants possessing sequences that are frequently reiterated. It is concluded that (Hind II/Hind III)-E sequences are frequently incorporated into SV40 defectively substituted genomes. (47 refs.)

77-5167 **DNA Synthesis by Partially Purified Replicating Simian Virus 40 Chromosomes.** (Eng) Edenberg, H. J. (Dept. Biological Chemistry, Harvard Medical Sch., Boston, MA 02115); Waqar, M. A.; Huberman, J. A. *Nucleic Acids Res* 4(9): 3083-3095; 1977.

A method is described for preparing partially purified Simian virus 40 (SV40) replicating chromosomes that are capable of continued DNA synthesis in vitro. A soluble DNA-synthesizing system is prepared from SV40-infected monkey cells, and the components are then sedimented through neutral sucrose gradients of very low ionic strength. SV40 chromosomes isolated from the gradient can synthesize DNA in vitro, indicating that the enzymes and other proteins required for this synthesis are bound to the replicating chromosomes. They should prove useful in characterizing the enzymes and other factors required for replication of SV40 and mammalian cell DNA. (21 refs.)

77-5168 **A Biochemical Method for Increasing the Size of Deletion Mutations in Simian Virus 40 DNA.** (Eng) Shenk, T. (Dept. Microbiology, Univ. Connecticut Health Center, Farmington, CT 06032). *J Mol Biol* 113(3): 503-515; 1977.

The size of the deletion mutations in the closed-circular, double-stranded DNA of a simian virus 40 (SV40) mutant was increased biochemically. Mutant and wild-type SV40 DNA's were treated with *Eco* RI restriction endonuclease to form full-length linear molecules. These molecules were then mixed, denatured, and annealed to re-form duplex structures. The linear heteroduplex DNA's were recircularized by treatment with DNA ligase to form closed-circular molecules, half of which contained a small deletion loop. The loops were cleaned with 51 endonuclease and the resultant linear molecules were used to infect permissive monkey kidney cells. The resulting viruses had deletions that were 45-90 base pairs larger than that of the original deletion mutant (*dl*892). Since the deletion of *dl* 892 is adjacent to a region of the SV40 genome that contains important regulatory sequences, stepwise extension of the deletion in *dl*892 into this region should allow identification of these functions. Most of the new mutants isolated, which were selected for viability, had deletions that extended almost entirely in the nonessential region, on the opposite side of the parental deletion. The one mutant with a deletion that extended into this regulatory region by 10 to 15 base pairs produced only 5% of the yield of wild-type virus. (29 refs.)

77-5169 **Initiation Points for DNA Replication in Nontransformed and Simian Virus 40-transformed Chinese Hamster Lung Cells.** (Eng) Martin, R. G. (Lab. Molecular Biology, Natl. Inst. Arthritis, Metabolism and Digestive Diseases, Bethesda, MD 20014); Oppenheim, A. *Cell* 11(4): 859-869; 1977.

A study was made of the initiation points for DNA replication in nontransformed Chinese hamster lung cells (CHL), CHL transformed by wild-type simian virus 40 [SV40 (CHLWT15)], and CHL transformed by the tsA239 and tsA30 mutants of SV40 (CHLA239L1, CHLA30L2). When grown in complete medium, CHLWT15 had more forks per unit length of DNA than did nontransformed CHL. In isoleucine-depleted medium, CHLWT15 had fewer forks per unit length than the few (1%-3%) nontransformed cells that continued DNA replication. When grown at permissive temperatures, CHLA239L1 and CHLA30L2 had more forks per unit length than nontransformed CHL in complete medium and fewer forks in depleted medium. At restrictive temperatures, the tsA-transformed cells behaved like nontransformed cells. These results are consistent with models that propose that the T antigen of SV40 initiates host DNA synthesis. They suggest that under depleted conditions, most nontransformed cells fail to synthesize a host initiator of DNA synthesis, but SV40-transformed cells continue to initiate DNA synthesis at T sites under the influence of T antigen. (32 refs.)

77-5170 **Mapping of Inverted Repeated DNA Sequences Within the Genome of Simian Virus 40.** (Eng.) Hsu, M. T. (Rockefeller Univ., New York, NY 10021); Jelinek, W. R. *Proc Natl Acad Sci USA* 74(4): 1631-1634; 1977.

Form I simian virus 40 (SV40) DNA cleaved with either *Escherichia coli* restriction endonuclease RI or with *Haemophilus parainfluenzae* restriction endonuclease II. The linear, double-stranded products were denatured by boiling, and the resulting single-stranded DNA was observed by electron microscopy to visualize regions of secondary structure. The most easily distinguishable structure was "rabbit ears" (2 hairpin loops) seen at position 0.11-0.30 on the map of the SV40 genome. Regions of inverted repeated sequences that also formed hairpin loops were found at positions 0.47-0.53 (I), 0.63-0.68 (II), 0.70-0.76 (III), and 0.90-0.96 (IV). All regions of hairpin loops could cross hybridize with one another. The 3′ and 5′ ends of the SV40 early and late messenger RNA's were located within regions of inverted repeated DNA sequences, where recombination events frequently occur. A map of the SV40 genome is illustrated. (28 refs.)

77-5171 **The Isolation of Tubulin and Actin from Mouse 3T3 Cells Transformed by Simian Virus 40 (SV3T3 Cells), an Established Cell Line Growing in Culture.** (Eng) Weber, K. (Abteilung Biochemie, Max-Planck-Institut fur Biophysikalische Chemie, Am Fassberg, D-3400 Gottingen-Nikolausberg, W. Germany); Koch, R.; Herzog, W.; Vandekerckhove, J. *Eur J Biochem* 78(1): 27-32; 1977.

A procedure for the rapid isolation of pure tubulin and actin from the same batch of tissue culture cells is described, along with a fingerprint analysis of actin from mouse 3T3 cells transformed by simian virus 40 (SV3T3 cells) and from beef skeletal muscle. Tubulin was prepared from SV3T3 cells by several cycles of temperature-dependent polymerization and depolymerization. The purity of the best preparations was about 95% according to sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Electron microscopy of the final product revealed numerous morphologically normal microtubules. SV3T3 actin was purified as a side product of the tubulin preparation. It showed the same electrophoretic mobility as muscle actin and was > 90% pure. SV3T3 actin and beef skeletal muscle actin were compared by fingerprint analysis of the tryptic peptides obtained from performic acid-oxidized protein. The two actins showed a high degree of homology; only 5/25 spots visualized by fluorescamine showed a difference in chromatographic mobility. It is concluded that the purification procedure described permits the rapid isolation of actin and tubulin from the same batch of tissue culture cells in sufficient amounts for comparative biochemical studies. (31 refs.)

77-5172 **Division of BALB/c Mouse 3T3 and Simian Virus 40-transformed 3T3 Cells in Cellular Aggregates.** (Eng) Carrino, D. (Dept. Biochemistry, Case Western Reserve Univ., Cleveland, OH 44106); Gershman, H. *Proc Natl Acad Sci USA* 74(9): 3874-3878; 1977.

Mitotic changes in BALB/c 3T3 cell cultures and Simian virus 40 (SV40) transformed 3T3 cells in aggregate culture were investigated. 3T3 cells incorporated labeled thymidine at a rate 25% that of the same cells in logarithmic phase flat cultures and 16 times the rate of cells in stationary phase flat cultures. The corresponding figures for the transformed cells were 33% and 14 times. During a 2 hr incubation with labeled uridine and thymidine, it was noted that the nucleosides did not penetrate past the outer four to six layers of culture; penetration was 100% when the incubation was continued for 4 days. Further studies with doubling times and rates of cell loss confirmed that 3T3 normal and transformed cells have aggregate growth properties in agreement with their behavior in flat cultures. SV40 transformed cells retained their ability to proliferate in high cell density cultures to a greater degree than normal cells. However, both lines displayed an increased capacity to divide in aggregate culture as compared to confluent flat culture. This system enables the study of high density cell-cell interactions that approximate in vivo conditions. (14 refs.)

77-5173 **Rhythmic Glycolytic and Respiratory Enzyme Patterns of Normal and Virally Transformed WI-38 Cells (Meeting Abstract).** (Eng.) Lewis, N. J. (Univ. Illinois Medical Center, Chicago, IL 60612); Rutzky, L. P.; Arsenis, C.; Pamper, R. W. *In Vitro* 13(3): 197; 1977. (no refs.)

77-5174 **Changes in Surface Properties of Normal and Transformed Cells Caused by Tunicamycin, an Inhibitor of Protein Glycosylation.** (Eng) Duksin, D. (Dept. Biochemistry, Univ. Washington, Seattle, WA 98195); Bornstein, P. *Proc Natl Acad Sci USA* 74(8): 3433-3437; 1977.

When normal and virally transformed mouse (3T3) and human (WI-38) cells were incubated for 4 hr in the presence of 0.5 μg/ml tunicamycin (TM), there was a marked inhibition of incorporation of D-^{3}H-mannose into the macromolecules, both in the culture medium and in the cell layer. High levels of TM (1.0 μg/ml) produced a decrease in the growth rate of 3T3 cells and detachment and death in simian virus 40 (SV40)- and polyoma-transformed cells within 24 hr. When 3T3 cells were exposed to TM for a longer period (2-4 days), they changed from a epithelioid to an elongated and spindle-shaped morphology. Trypsinized or EDTA-detached, virally transformed cells showed a marked reduction in agglutination by concanavalin A, but agglutination by wheat germ or soy bean agglutinin was unaffected. A high-mol-wt protein, presumed to be related to fibronectin, was reduced markedly in the medium of cells cultured with TM. TM may interfere with the insertion or function of one or more cell-surface glycoproteins. These changes could affect a number of cell properties such as attachment, cell shape, and agglutinability. (38 refs.)

See also:

* (Rev.): 77-4841, 77-4842, 77-4843, 77-4844, 77-4845, 77-4846, 77-4847, 77-4848, 77-4849, 77-4869.
* (Chem.): 77-4895, 77-4896, 77-4933, 77-4939, 77-4993.
* (Phys.): 77-5021.
* (Immun.): 77-5176, 77-5181, 77-5183, 77-5185, 77-5186, 77-5187, 77-5188, 77-5189, 77-5190, 77-5191, 77-5194, 77-5195, 77-5199, 77-5215, 77-5217, 77-5222, 77-5227, 77-5228, 77-5229, 77-5233, 77-5234, 77-5235, 77-5239.
* (Path.): 77-5254.
* (Epid.): 77-5359.

IMMUNOLOGY

77-5175 **Immunogenetic Control of Brain Tumor Growth in Rats.** (Eng.) Albright, A. L. (Dept. Neurosurgery, Presbyterian Univ. Hosp., 230 Lothrop St., Pittsburgh, PA 15213); Gill, T. J.; Geyer, S. J. *Cancer Res* 37(8, part 1): 2512-2522; 1977.

The intracerebral and sc growth of a transplantable gliosarcoma was investigated in rats from each of the eight known histocompatibility (Ag-B) groups. The genetic control of brain tumor growth was studied by evaluation of intracerebral and sc gliosarcoma growth in backcross progeny of tumor-susceptible x tumor-resistant rats. Susceptibility to this type of growth correlated with histocompatibility type. Susceptibility was transmitted as a dominant trait, and at least two genes or gene complexes were involved: one linked to the major histocompatibility complex and one independent of it. The genetic mechanisms did not appear to be affected significantly by the tumor site. Antibodies of Ag-B1 histocompatibility antigens, which were those of the strain in which the tumor originated, and to tumor-associated antigens were generally present in animals whose tumor had regressed. Only tumor-specific antibodies appeared in the sera of Ag-B1 animals that had the tumor. A cytotoxic lymphokine was present in the sera of tumor-bearing animals, but its level did not correlate with tumor growth or regression. It is concluded that tumor susceptibility is under polygenic control, that the genetic mechanisms regulating susceptibility to tumor growth are not affected significantly by site, and that the tumor cells carry histocompatibility antigens and tumor-associated antigens, despite the fact that they were derived from brain tissue. (43 refs.)

77-5176 **Host Control of Tumor Growth.** (Eng.) Ting, C. C. (Lab. Cell Biology, NCI, NIH, Bethesda, MD 20014); Tsai, S. C.; Rogers, M. J. *Science* 197(4303): 571-573; 1977.

The effect of FBL-3 ascitic fluid of mice bearing ip tumors, pleural effusions from human breast cancer, and benign ascitic fluid from C57BL/6 mice on the growth of FBH-3 cells in vitro and in vivo was investigated. The humoral factor in the ascitic fluid of tumor-bearing mice and in the pleural effusion had a mol wt of 40,000 to 60,000. It suppressed cell-mediated tumor immunity and promoted murine tumor growth. However, hosts that recover from the immunosuppressive effect produce substances in their serum that neutralize the immunosuppressive factors. These factors may play an important role in the control of tumor growth. (9 refs.)

77-5177 **Systemic Alteration Induced in Mice by Ultraviolet Light Irradiation and Its Relationship to Ultraviolet Carcinogenesis.** (Eng.) Fisher, M. S. (Basic Res. Program, NCI, Frederick Cancer Res. Center, P. O. Box B, Frederick, MD 21701); Kripke, M. L. *Proc Natl Acad Sci USA* 74(4): 1688-1692; 1977.

A series of experiments conducted on C3H/HeN (MTV-) mice that received a regimen of UV irradiation (av dose rate 2.8 joules/m^2 for 1 hr, 3 times per week, for a minimum of 3 mo) demonstrated an immunologic defect in these mice that precedes the development of primary skin cancers. Formation of a common circulation or parabiosis between normal and UV-treated mice followed by tumor challenge with UV-induced syngeneic fibrosarcomas resulted in progressive tumor growth in both mice. This suggests an active suppression exerted by the UV-treated mice on their nonirradited partners. When 5×10^7 lymphoid cells were transferred from UV-irradiated mice to lethally x-rayed recipient (850 rads, 24 hr before transfer), recipients were unable to reject tumor challenge. Thus, lymphoid cells from UV-treated mice lack the capacity to mediate tumor rejection in vivo. Under conditions in which cells from tumor-implanted, nonirradiated mice were highly cytotoxic in vitro against UV-induced tumors, splenic lymphocytes from tumor-implanted, UV-treated donors failed to show cytotoxicity. Possible mechanisms by which UV-irradiation induces this systemic alteration in mice that causes them to accept highly antigenic tumors are discussed. (13 refs.)

77-5178 **Monitoring of Immunosuppression in Beagles.** (Eng.) Benfield, J. R. (Professional Staff Assoc., 1124 W. Carson St., Torrance, CA 90502); Shors, E.; Schick, P.; Byfield, P. E.; Okita, M. *J Surg Res* 23(3): 207-214; 1977.

A method for evaluating immunosuppression in dogs was developed and used to study the effects of azathioprine (AT) and corticosteroids on beagles. Benzo(a)pyrene (BP) was injected into the bronchial submucosa of beagle dogs in 21 weekly aliquots of 15 mg up to a total of 315 mg. After that, weekly topical applications of 5 mg of N-methyl-N-nitrosourea (NMU) were given. High-dose immunosuppression (MIS) consisted of AT at 2.5 mg/kg/day and methylprednisolone at 1 mg/kg/day. Low-dose immunosuppression (LIS) consisted of AT at 1.2 mg/kg/day and methylprednisolone at 0.4 mg/kg/day. The effects of immunosuppression were measured after 2, 5, and 9 mo of treatment. Antibody titers to bovine RBC, rat RBC, and chicken γ-globulin were determined, and skin allografts were used to test immunity levels. Delayed cutaneous hypersensitivity responses to rabies vaccine, combination distemper-hepatitis-leptospirosis vaccine, and 3,5-dinitrochlorobenzene (DNCB) were also evaluated. Absolute lymphocyte counts were the most sensitive dose-related nonspecific indicator of the level of immunosuppression. HIS depressed antibody responses within 2 mo, prolonged skin allograft rejection from 6.5 to 14.1 days, and suppressed cutaneous responses to distemper vaccine and DNCB. Most beagles could not tolerate chronic HIS, but LIS was well-tolerated. LIS prolonged skin allograft rejection to 10.8 days, suppressed cutaneous hypersensitivity, and inhibited antibody responses after 9 mo but not after 2 mo of treatment. The skin tests all provided evidence of immunosuppression in LIS but none did so consistently. Distemper vaccine gave the clearest responses. (6 refs.)

77-5179 **Abolition of Immunodepression Caused by 1,2-Dimethylhydrazine in Rats by Phenformin Treatment.** (Rus) Dil'man, V. M. (Lab. Endocrinology, N. N. Petrov Scientific Res. Inst. Oncology, USSR Ministry Health, Leningrad, USSR); Sofronov, B. N.; Anisimov, V. N.; Nazarov, P. G.; L'vovich, E. G.; Polushina, L. I. *Vopr Onkol* 23(8): 50-54; 1977.

The effect of phenformin treatment on 1,2-dimethylhydrazine (DMH)-induced immunodepression in rats was examined. Treatment of the rats with 21 mg/kg DMH once a wk for 4 wk resulted in a decrease in the biogenic amine level (particularly dopamine in the hypothalamus), a decrease in glucose tolerance, and an increase of insulin and triglycerides in the blood. It is suggested that DMH immunodepression resembles that which occurs during aging and pregnancy. Administration of 2 mg/day phenformin po restored cell-mediated immune response and phagocytic activity. (19 refs.)

77-5180 **Tumor Development During Immunosuppressive Therapy of NZB/NZW Autoimmune Disease (Meeting Abstract).** (Eng.) Sullins, D. (Univ. Missouri, Columbia, MO 65201); Morris, A. D.; Jones, M.; Buchert, P.; Moeschberger, M. *Clin Res* 25(4): 584A; 1977. (no refs.)

77-5181 **Activation of K Cells in Mice with Transplanted Tumours Differing in Immunogenicity and Metastasizing Capacity.** (Eng) Mantovani, A. (Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62-20157, Milan, Italy); Polentarutti, N.; Alessandri, G.; Vecchi, A.; Giuliani, F.; Spreafico, F. *Br J Cancer* 36(4): 453-460; 1977.

Antibody-dependent cellular cytotoxicity (ADCC) was evaluated in BALB/c mice with transplanted Moloney sarcoma virus-induced tumors T-MSV and MS2, and in C57BL/6 mice with transplanted FS6 chemically-induced sarcoma, Lewis lung carcinoma and B16 melanoma. Tumor-bearing animals showed higher levels of ADCC than normal mice. Experiments with BALB/c mice showed that K cell activation was characterized by a significant increase in splenocyte cytotoxicity on day 7 that reached its peak on day 14. These levels remained high until day 28 when observation was halted. Splenocytes from animals with T-MSV tumors (immunogenic, spontaneously regressing) appeared more effective than those from animals with MS2 tumors (poorly immunogenic, metastasizing) except on day 28, when cytotoxicity was similar in both groups. These observations were confirmed in C57BL/6 mice. In tests with T-MSV and FS6 sarcomas, carbonyl iron significantly reduced K cell activity of normal and tumorous splenocytes; but spleen cells from tumor bearing mice still had higher levels of ADCC than similarly treated normal lymphoid cells. The biological mechanisms responsible for these findings are unclear. (32 refs.)

77-5182 **Transplantable Mammary Tumors in Wistar/Furth Rats: Development, Antigenicity, and Effect of Hormone Manipulations.** (Eng.) Piessens, W. F. (Dept. Medicine, Robert B. Brigham Hosp., 125 Parker Hill Ave., Boston, MA 02120); Churchill, W. H. *J Natl Cancer Inst* 59(3): 911-918; 1977.

Transplantable tumor lines were developed from 7,12-dimethylbenza(a)anthracene (DMBA)-induced mammary tumors in virgin inbred female W/Fu rats. Although the primary tumors regressed following oophorectomy, the growth of late generation transplantable lines was unaffected by castration or by injections of testosterone (5 mg, weekly) or weekly 17β-estradiol (5 μg) plus progesterone (5 mg). This result coincided with a change in tumor morphology from well- to poorly differentiated anaplastic tumors. The transplantable tumors stimulated syngeneic lymphocytes in mixed lymphocyte-tumor cell cultures. However, prior sensitization by excision of a first tumor graft failed to protect the animals against a second challenge with cells from the same tumor line. It is suggested that these transplantable tumor lines are poorly immunogenic in vivo. (31 refs.)

77-5183 **Lymphoid Cell Lines: In Vitro Cell Markers in Correlation to Tumorigenicity in Nude Mice.** (Eng) Diehl, V. (Div. Haematology, Dept. Internal Medicine, Univ. Cologne, D-5000 Cologne, W. Germany); Krause, P.; Hellriegel, K. P.; Busche, M.; Schedel, I.; Laskewitz, E. *Haematol Blood Transfus* 20: 289-296; 1977.

A cytogenetic marker, the 14q+ translocation, was correlated to the ability of lymphoblastoid cell lines (LCL) to form tumors in nude mice in order to differentiate between nonneoplastic LCL derived from malignant and nonmalignant tissue, and neoplastic lymphoma and myeloma lines exclusively originating from neoplastic tissue in vivo. In particular, cell cultures initiated with or without the addition of exogenous Epstein-Barr virus (EBV), cell lines derived from patients with Hodgkin's disease, and lines originating from lymphomatous tissue with lymphoma-type cell characteristics were examined. LCL lacking the 14q+ marker failed to produce tumors upon xenotransplantation (sc on im) in concentrations of 1 x 10^6 cells per inoculum into nude mice. Lymphoma-type lines of Burkitt's lymphoma, lymphosarcoma, and Hodgkin's disease origin, genotypically aneuploid and expressing the 14q+ marker, were tumorigenic in nude mice. Tumor growth in nude mice was independent of the presence of EBV in the inoculated cells. However, one factor that might invalidate the role of tumorigenicity in allogeneic hsots as a reliable oncogenic marker is the route of inoculation. LCL might produce tumors, even in small inocula, when injected intracerebrally, thus possibly bypassing blood cell-mediated defense mechanisms. (21 refs.)

77-5184 **Studies of Cellular Tumorigenicity in Nude Mice (Meeting Abstract).** (Eng.) Freedman, V. H. (Yeshiva Univ., New York, NY 10033). *Diss Abstr Int [B]* 38(4): 1550-1551; 1977. (no refs.)

77-5185 **Biological Characterization of a Tumour-Growth-promoting Factor from Ascitic Fluid of Tumour-bearing Mice.** (Eng.) Henriksen, O. (Lab. Cell Biology, NCI, NIH, Bethesda, MD 20014); Law, L. W. *Int J Cancer* 19(6): 866-869; 1977.

The tumor-growth-promoting activity in the ascitic fluid of mice with progressively growing simian virus 40 (SV40)-induced tumors was studied. mKSA cells (an SV40-transformed neoplasm of BALB/c mice) were injected sc (5×10^4 cells) in the leg of 3- to 4-wk-old BALB/c mice. After 3-4 wk, the tumor-bearing legs were amputated. Secondary tumor challenge (5×10^4 mKSA cells) was given sc in the flank. Ascitic fluid or serum was injected sc in the back. In contrast to the low tumor frequency seen after secondary tumor challenge at 10-15 days after amputation (6.3%), daily injections of mKSA ascitic fluid increased the tumor frequency to 85%. Fluid derived from another tumor L1210 (a chemically induced lymphoma of DBA/2 mice) also prolonged the eclipse phase, the immunologically nonresponsive state indicating that the active component acts nonspecifically. The active ascitic component was also present in serum from tumor-bearing animals but not in serum from normal animals. When cell-free ascitic fluid from mKSA tumor-bearing mice was administered to BALB/c mice together with an inoculum of a low, normally nontumorigenic dose of SV40-transformed tissue culture cells, these cells grew progressively and eventually killed the animals. These data suggest that mKSA and L1210 cell-free ascitic fluids contain a component that is able to prolong the immunologically paralyzed state of tumor-bearing animals, but is not able by itself to induce the eclipse phase. It is suggested that the eclipse phase can only be reached via a continuous interaction between tumor cells and their host. (11 refs.)

77-5186 **Immunostimulation of Syngeneic Sarcoma Growth Induced Primarily in Mice with Simian Adenovirus SA7 (C8).** (Rus) Ageenko, A. I. (P. A. Gertsen Res. Inst. Oncology, Moscow, USSR); Erkhov, V. S. *Vopr Onkol* 23(8): 57-60; 1977.

A marked decrease in the latent period of tumor development was noted following transplantation of splenic cells from CBA mice bearing the simian adenovirus (SA)7 (C8) primary sarcoma together with autologous sarcoma cells into syngeneic recipients irradiated with 600 rads. Pretreatment of normal and tumor-bearing mice with 6 mg/100 g body wt hydrocortisone did not reduce the immunostimulation of tumor growth by spleen cells. (13 refs.)

77-5187 **Factors Interfering with Cellular Immunological Responses to the Murine Mammary Tumor Virus in Tumor-bearing Mice.** (Eng.) Creemers, P. (Radiobiological Inst. TNO, 151 Lange Kleiweg, Rijswijk, Netherlands); Brinkhof, J. *Int J Cancer* 20(3): 441-447; 1977.

BALB/c mice bearing virally induced mammary tumors showed cellular immunity to murine mammary tumor virus (MTV) in the lymphocyte blastogenesis (LB) and leukocyte adherence inhibition (LAI) tests. T-cell-enriched spleen cell fractions from tumor-bearing mice became unresponsive with progressive tumor growth in the LB test using purified MTV as antigen. However, extensive washings (8) or mild trypsinization was able to restore responsiveness. This wash fluid was also found to be capable of inhibiting the MTV-specific blastogenesis by other cells. The washing of spleen cells from tumor-bearers inhibited the LAI reactivity of immunized donors. In addition, sera from tumor-bearing mice had blocking activity in the LAI assay, and they inhibited MTV-specific blast formation in the LB test. Both MTV and anti-MTV antibodies were detected in the spleen cell washing fluid from the tumor-bearing mice. The suppressive mechanisms of the blocking serum and spleen cell washing may be due to antigen-antibody complexes. (21 refs.)

77-5188 **Delayed Foreign-Body Tumorigenesis in Mice Infected with Lactate Dehydrogenase-elevating Virus: Brief Communication.** (Eng.) Brinton-Darnell, M.

Wistar Inst., 36th and Spruce Sts., Philadelphia, PA 19104); Brand, I. *J Natl Cancer Inst* 59(3): 1027-1029; 1977.

Delayed foreign-body (FB) tumorigenesis was studied in mice nfected with lactate dehydrogenase-elevating virus (LDV). Eight-week-old CBA/H mice of both sexes were infected ip with LDV (10^3 ID50's). Two weeks later, these mice and noninfected controls received double sc implants of unplasticized vinyl chloride-vinyl acetate copolymer films (0.2 x 15 x 22 mm). FB tumorigenesis was delayed by 2 mo in infected nimals of both sexes. Since cellular immunity is not known to influence the course of FB tumorigenesis, these results could not be explained by an LDV effect on cellular immunity. (35 refs.)

77-5189 **Dissociation of Antiviral and Antitumor Immunity in Resistance to Marek's Disease.** (Eng.) Powell, P. C. (Houghton Poultry Res. Station, Houghton, Huntingdon, Cambridgeshire PE17 2DA, England); Rowell, J. G. *J Natl Cancer Inst* 59(3): 919-924; 1977.

The relation between antiviral and antitumor immunity in Marek's disease (MD) was studied in HPRS Rhode Island Red chickens. Immunization with glutaraldehyde-inactivated chicken kidney cells infected with MD virus suppressed both viral replication and antigen production after challenge with virulent virus. Lymphocytes specifically cytotoxic to cells bearing MD tumor antigens could not be detected. Immunization with glutaraldehyde-inactivated cells of MD lymphoma-derived continuous lymphoblastoid cell lines that were protected against MD left viral replication unaffected. At the same time, there was evidence of stimulated cell-mediated immunity. This supports the view that immunity to MD may be directed against either virus- or tumor-specific antigens and that both mechanisms may be operative in natural resistance to this disease. (33 refs.)

77-5190 **Murine Mammary Tumor Virus Protein Vaccine: Induction of Antivirus Immunity and Inhibition or Acceleration of Growth of Transplanted Mammary Tumors.** (Eng.) Creemers, P. (Tumor Virology Branch, Rep-Inst. Organisation Health Res. TNO, 151 Lange Kleiweg-Rijswijk (ZH), Netherlands); Ouwehand, J.; Bentvelzen, P. *J Natl Cancer Inst* 59(3): 895-903; 1977.

The induction of antivirus immunity and the growth of transplanted mammary tumors were studied in 12-wk-old mice vaccinated with a protein fraction of murine mammary tumor virus (MuMTV) enriched for the major glycoprotein gp52. Twenty days after vaccination, BALB/c mice were challenged with live MuMTV-induced tumor cells and DBAf mice with live MuMTV-positive leukemia L1210 cells. Alum and interphase materials isolated from *Mycobacterium smegmatis* (IPM) were used as adjuvants. Control animals were given the adjuvants alone. In BALB/c mice given 1 μg of the gp52-enriched fraction precipitated on alum, tumorigenesis was delayed by 10 wk. A dose of 10 μg had no clear effect, but 100 μg accelerated tumor growth. Each of the vaccinated animals developed a tumor vs only 60% of the controls. In DBAf mice, low doses of the vaccine accelerated tumor growth, generally in a dose-dependent manner. The use of 50 μg IPM and the gp52-enriched fraction resulted in protection, but a combination with 100 μg IPM accelerated tumor growth. Protection was observed when serum blocking factors were absent, even when cellular immune reactivity and the antibody titer were low. In the presence of serum blocking factors, protection was observed only with high antibody titers and strong cellular immunity. (29 refs.)

77-5191 **Immunoprevention of X-Ray-induced Leukemias in the C57BL Mouse.** (Eng.) Peters, R. L. (Microbiological Associates, Walkersville, MD 21793); Sass, B.; Stephenson, J. R.; Al-Ghazzouli, I. K.; Hino, S.; Donahoe, R. M.; Kende, M.; Aaronson, S. A.; Kelloff, G. J. *Proc Natl Acad Sci USA* 74(4): 1697-1701; 1977.

Attempts were made to prevent x-ray-induced leukemias by inducing immunity to endogenous C-type virus in C57BL/6N female mice (30-36 days old). Prior to and following irradiation with four weekly treatments of 150 rads each, some mice were actively immunized with either inactivated Rauscher murine leukemia virus (R-MuLV) or inactivated Gross MuLV. Passive immunity treatments were given to mice using goat anti-Gross-MuLV IgG before, during, and after irradiation. Simian sarcoma virus, normal IgG, and complete Freund's adjuvant were used in controls. A significant reduction in total tumor incidence and a higher amount of anti-AKR-gp70 (70,000-dalton glycoprotein) antibody were observed in the R-MuLV-immunized active group and the immune-IgG-treated passive group, compared with other experimental and control groups. In addition, tissues from these two groups showed a significantly low incidence of isolatable virus. The data support the viral etiology of irradiation-induced tumors and further establish that neoplastic disease may be prevented by immune regimens directed against the cocarcinogenic effect of endogenous C-type virus. (24 refs.)

77-5192 **Immunization of Guinea Pigs Against L_2C Leukemia with Live Leukemic Cells by Intradermal Inoculation: Early and Late Effects.** (Eng.) Gross, L. (Cancer Res. Unit, Veterans Admin. Hosp., Bronx, NY 10468); Dreyfuss, Y. *Fed Proc* 36(9): 2272-2276; 1977.

This study was made to determine whether id inoculation of strain 2 guinea pigs with live L_2C leukemic cells could confer immunity to a subsequent challenge of L_2C cells. Doses of approx 1-83 cells produced id tumors in 135/306 animals; the tumors in 54 animals regressed spontaneously. However, 23/54 animals developed, after 1-4.5 mo, lymphosarcomas in the spleen, liver, and mesenteric lymph nodes. Resistance could be substantially increased by a second booster inoculation. Previous studies yielded similar results. Another series of 91 immunized guinea pigs (in which id tumors also regressed) were challenged by sc injections of massive doses of leukemic cells (0.5 ml of 10^{-2} dilution). Only 7 animals (1/55 females; 6/36 males) developed leukemia initially, within 15-33 days; 4 more animals developed leukemia after 5, 9, 17, and 29 mo. Contrasted with these results was the finding that sc injection of leukemic cells (0.5 ml of 10^{-2} to 10^{-6} dilutions) into nonimmunized guinea pigs resulted in the development of leukemia and death of 460/467 animals with an av latency of 14 days for tumor development and 23 days for death from leukemia. Thus, specific immunity against L_2C leukemia can be induced in strain 2 guinea pigs by id injection of small doses of live L_2C leukemic cells. However, the injection must be followed by the development and subsequent spontaneous regression of a small id tumor at the injection site. (13 refs.)

77-5193 **Mechanisms Operative in LPS-induced Tumor Protection in Mice (Meeting Abstract).** (Eng.) Berendt, M. J. (Hahnemann Medical Coll. and Hosp., Philadelphia, PA 19102). *Diss Abstr Int [B]* 38(4): 1644; 1977. (no refs.)

77-5194 **Prevalence of Type-specific Antibody Against Type 1 and Type 2 Herpes Simplex Virus in Women with Abnormal Cervical Cytology; Evidence Towards Pre-pubertal Vaccination of Sero-negative Female Subjects.** (Eng) Skinner, G. R. (Dept. Medical Microbiology, Univ. Birmingham, Medical Sch. Birmingham, B15 2TJ, England); Whitney, J. E.; Hartley, C. *Arch Virol* 54(3): 211-221; 1977.

The prevalence of type-specific antibodies against types 1 and 2 herpes simplex virus (HSV) in women with abnormal uterine cervical cytology, including cervical carcinoma, was compared with that of patients with negative cervical cytology and patients with carcinoma of other body sites. Patients with cervical dysplasia, invasive cervical carcinoma, carcinoma in situ, and a suspicious cervical cytology had significantly higher ($p < 0.05$) prevalences of type 2-specific antibody than control patients. Furthermore, patients with invasive cervical carcinoma had a striking prevalence of type 2-specific antibody (80%) that was more than twice that in patients with preinvasive cervical carcinoma or suspicious cervical cytology. In simultaneous case-control matching for age and socioeconomic class, type 2-specific antibody was present in 33% of patients with abnormal cervical cytology but in only 9% of control patients ($p < 0.05$). Patients with type 2-specific antibody only were more prevalent in cases with abnormal cytology. The relative overall infrequency (7%) of subjects with type 2-specific antibody only was noted. Coexisting types 1- and 2-specific antibody were significantly more prevalent in patients with positive cervical cytology. In contrast, patients with type 1-specific antibody only were significantly less common in cases with abnormal cervical cytology. These findings suggest that prepubertal exposure to type 1 HSV might offer some "protection" to premalignant and malignant cervical changes, perhaps by preventing or modifying postpubertal type 2 cervical infection. (24 refs.)

77-5195 **Cell-mediated Response to Simian Oncornaviruses in Women During Pregnancy (Meeting Abstract).** (Eng.) Thiry, L. (Institut Pasteur du Brabant, Brussels, Belgium); Sprecher-Goldberger, S.; Bossens, M.; Neuray, F. *Br J Cancer* 36(3): 410-411; 1977. (no refs.)

77-5196 **Inhibition by Sera and Soluble Antigens of T-Cell-Mediated Cytotoxicity Against Leukaemia-Associated Antigens.** (Eng.) Ting, C. C. (Lab. Cell Biology, NCI, NIH, Bethesda, MD 20014) Rogers, M. J. *Nature* 266(5604): 727-729; 1977.

Antigen inhibition of T-cell mediated cytotoxicity using pooled lymph node and spleen (C57BL/6 (B6) mouse) cells against leukemia-associated antigens is investigated. The pooled effector cells from B6 mice immunized with a syngeneic Friend virus-induced lymphocytic leukemia (FBL-3) killed both syngeneic FBL-3 target cells (49% net lysis) and HFL/d-tc Friend virus-induced leukemia target cells (18% net lysis) as measured by a 20-hr ^{125}I-uridine deoxyribose release assay (IRA). Conversely, alloantisera of the appropriate specificity and syngeneic serum against FBL-3 tumor cells inhibited cytotoxicity ($p < .001$). Mouse sera tested for binding to FBL-3 cells and inhibition of cytotoxicity against FBL-3 cells had the following activities in decreasing order: anti-H-2b, anti-FBS, anti FBL-3, and anti-Ia. Only pretreatment with syngeneic anti-FBL-3 serum specifically reduced the cytotoxic response to FBL-3 cells in the syngeneic B6 host. In IRA tests of effects on the cell-mediated cytotoxic reaction to FBL-3, 7.5 μg/ml papain-soluble FBL-3 antigen completely inhibited cytotoxicity, 2.5-12.5 μg/ml purified viral protein gp 70 gave a 20-30% inhibition, and 50 μg/ml papain-soluble H-2b antigen gave no inhibition. The need for sensitizing cells, effector cells, and target cells to be syngeneic at the H-2 locus and the hypothesis that tumor-associated antigens may be of the H-2 type are not supported by these data. (17 refs.)

77-5197 **Detection of Soluble Tumor-associated Antigens in Serum of Tumor-bearing Rats and Their Immunological Role In Vivo.** (Eng.) Rao, V. S. (Dept. Pharmacology and Medicine, Yale Univ. Sch. Medicine, New Haven, CT 06510); Bonavida, B. *Cancer Res* 37(9): 3385-3389; 1977.

Soluble tumor antigens were detected in the serum of tumor-bearing rats, and the effect of presensitization of W/Fu rats with these antigens was investigated. Sublethally irradiated (500 R) rats were inoculated sc with 5 x 10 syngeneic C58(NT)D Gross virus-induced lymphoma cells. Soluble antigens were assessed by specific inhibition of the complement-mediated cytotoxicity of isogenic W/Fu anti-C58(NT)D antibodies against ^{51}Cr tumor target cells. Circulating tumor antigens were first detected 8 days after inoculation and reached a max concentration by 13-14 days, which coincided with max tumor growth. This was followed by the sudden death of the animals. Pooled serum from tumor-bearing rats obtained 13 days after inoculation was fractionated on Sephadex G-150 to give three peaks, one of which contained all of the antigenic activity. Fractionation of serum from 500-R-treated non-tumor-bearing rats did not show antigenic activity in any of the peaks. The mol wt of the antigenic fraction was 50,000-60,000 daltons. Presensitization of normal rats with soluble tumor antigens resulted in a significant enhancement of tumor growth that was dependent on antigen concentration. The enhancement was specific, since rats pretreated with serum from 500-R-irradiated rats or from 500-R-irradiated and WR-6- (a syngeneic but antigenically unrelated lymphoma) tumor-bearing rats behaved similarly to control rats. The enhancement was observed only when the serum circulating antigen was injected before tumor inoculation. This indicates that the antigen acts on virgin precursor immunocompetent cells. The demonstration that sensitization to soluble tumor antigen may lead to adverse effects on tumor rejection cautions against the generalized use of soluble antigen in antitumor immunotherapy. (30 refs.)

77-5198 **Soluble Tumor Antigen-induced Lymphocyte Proliferation: Effects of Serum from Normal and Tumor-bearing Mice.** (Eng.) Calderwood, M. B. (Dept. Pathology, Univ. Florida Coll. Medicine, Gainesville, FL 32610); Forbes, J. T.; Smith, R. T. *Int J Cancer* 20(3): 400-407; 1977.

The effects of serum from tumor-bearing mice on tumor-specific proliferative responses to soluble tumor antigens are described. Antigens solubilized from methylcholanthrene-induced fibrosarcomas induced proliferation by spleen and lymph node cells from tumor-bearing C57BL/6 and B10.D2 mice. Low concentrations ($\leq$2.5%) of serum from tumor-bearing animals markedly inhibited the antigen-induced proliferation when the soluble antigen was homologous or syngeneic. Tumor-bearing sera inhibited only tumor antigen-induced proliferation and not proliferative responses to phytohemagglutinin and alloantigens. The advantages of the lymphoproliferative assay over other assays for the detection of blocking factors are pointed out. (38 refs.)

77-5199 **Tumour-specific Transplantation Antigen from SV40 Transformed Cells Binds to DNA.** (Eng.) Chang, C. (NCI, NIH, Bethesda, MD 20014); Luborsky, S. W.; Mora, P. T. *Nature* 269(5627): 438-440; 1977.

Studies were performed to characterize the tumor-specific transplantation antigen (TSTA) from SV40 transformed murine SV AL/N cells. The TSTA and T antigen co-purified through ammonium sulfate precipitation and DEAE- and DNA-cellulose column chromatography. Both the T and TSTA specific activities were enriched through binding to DNA. Purified antigen was found to provide immunity against 10- to 100-fold tumorigenic doses of mKSA-ASC tumor cell challenge when administered at the 1 μg level. The TSTA antigen also bound to double-stranded calf thymus DNA. These findings provide further support for the homology between T antigens and TSTA. (21 refs.)

77-5200 **Tumor-specific Transplantation Antigens in Spontaneously Transformed Hamster Cell Lines.** (Eng.) Yaniv, A. (Dept. Human Microbiology, Sackler Sch. Medicine, Tel-Aviv Univ., Ramat-Aviv, Tel-Aviv, Israel); Gotlieb-Stematsky, T.; Eylan, E. *Cancer* 39(4): 1450-1454; 1977.

Tumor rejection tests demonstrated the presence of individual distinct tumor specific transplantation antigens in each of the spontaneously transformed hamster embryo cell lines tested as well as in cell lines derived from tumors induced in hamsters by these transformed cells. Immunoprotection resulted in 70-100% of hamsters challenged with a minimal dose of cells required to induce tumors in all animals. (20 refs.)

77-5201 **Influence of HLA, ABO, and Rh(D) on Survival after Remission in Acute Myelogenous Leukaemia (Letter to Editor).** (Eng.) Harris, R. (Dept. Medical Genetics, St. Mary's Hosp., Manchester M13 0JH, England); Zuhrie, S. R.; Taylor, G. M.; Freeman, C. B.; Wentzel, J.; Geary, C.; MacIver, J. E. *Lancet* 2(8039): 653; 1977.

The influence of HLA (histocompatibility antigen), ABO (blood group), and Rh(D) (Rhesus factor D type) on survival was studied in acute myelogenous (AML) patients (142, 183, and 173 patients, respectively, with 100 normal controls in each study group). HLA-B12 was associated with resistance to AML. The ABO locus, through its association with HLA phenotype A2 and B12, appeared to be involved in the prognosis of AML. There were no Rh(D)-negative patients with erythroleukemia, and a poor remission rate in Rh(D)-negative patients with morphological variants of AML. These associations could be artefacts because of the small sample size. (6 refs.)

77-5202 **HLA and MLC Typing in Patients with Hodgkin's Disease.** (Eng) Hansen, J. A. (Memorial Sloan-Kettering Cancer Center, New York, NY 10021); Young, C. W.; Whitsett, C.; Case, D. C.; Jersild, C.; Good, R. A.; Dupont, B. *Prog Clin Biol Res* 16: 217-227; 1977.

Major histocompatibility (HLA) antigen typing for 27 A- and B-locus antigens was performed in 137 Caucasian patients with Hodgkin's disease. The A- and B-locus-antigen frequencies were composed for the entire group of patients, for 51 of these patients studied in a prospective manner, and for 62 of these patients surviving with Hodgkin's disease for > 5 yr. HLA-D typing by the mixed lymphocyte culture (MLC) test for three HLA-D specificity groups (DW2, DW3, and DW4) was performed in 51 unselected Caucasian patients. HLA-AW33 was found in 0% of these patients and in 5.9% of 321 random Caucasian blood donors, a difference that is statistically significant ($p < 0.01$). HLA-A1 was significantly increased to 35.8% in the entire patient group ($N = 137$) compared to 25.4% in 855 random North American Caucasians ($p < 0.02$). There was no significant deviation of any A- or B-locus antigen in relation to sex, histology, age of the patient, or duration of survival (newly diagnosed vs 5-yr survivors). No significant deviation for any of the three common HLA-D determinants (DW2, DW3, or DW4) was seen. (18 refs.)

77-5203 **Distribution of HLA-A, B, C and the Merrit B-Cell Alloantigen Specificities in Chronic Lymphatic Leukemia.** (Eng) Gossett, T. (Dept. Pathology, Sch. Medicine, Univ. California, Los Angeles, CA 90024); Walford, R.; Gatti, R. M. *Prog Clin Biol Res* 16: 55-63; 1977.

Reactions with panels of normal peripheral B lymphocytes and chronic lymphocytic leukemia (CLL) cells revealed 3 new specificities of the Merrit B cell alloantigenic system, bringing the number of provisionally designated specificities to 22. This system of antigenic determinants is well-represented on normal B lymphocytes and has a distribution that is roughly similar to that of the CLL panel. No significant differences in antigen frequencies of the A, B, and C loci of the HLA complex between normal and CLL cells were seen. However, certain specificities may have significantly different distributions on the two different panels. Merrit Groups 17, 18, and 22 appeared to be more frequently expressed on the B cells than on the CLL cells tested, and Group 16 seemed to be more frequently expressed on the CLL cells. Likewise, C-locus specificities 2, 3, 4, and 5 were more frequently expressed on the CLL cells than on normal cells. Although these differences are statistically significant ($p < 0.05$), the number of cells tested was low. (36 refs.)

77-5204 **HLA Associations with Acute Myelogenous Leukemia.** (Eng) Parrish, E. J. (Dept. Microbiology, Bowman Gray Sch. Medicine, Winston-Salem, NC 27103); Heise, E. R.; Cooper, M. R. *Prog Clin Biol Res* 16: 81-89; 1977.

An investigation of the possible association of human acute granulocytic leukemia (AGL) with the major histocompatibility complex (HLA) revealed that certain HLA phenotypes and haplotypes may be associated with AGL and with a favorable response to therapy. The study group consisted of 57 Caucasian patients (32 men, 25 women) with newly diagnosed acute myelocytic leukemia and acute myelomonocytic leukemia. There were no statistically significant differences in the frequencies of individual HLA-A and B locus antigens between AGL patients and healthy controls. With the hypothesis that leukemia is a multigenic disease, groups of two or more antigens were tested for deviation from the frequencies in the control group. Five phenotypes consisting of various combinations of A1, A3, Bw17, and Bw35 were in significant excess in the patient group. Three combinations represent the potential haplotypes A1, Bw17; A1, Bw35; and A3, Bw35. A1, Bw17 and A3, Bw35 were positively associated with the control group, but A1, Bw35 was negatively associated with the control group. The study also revealed that HLA-B12 was significantly more frequent in AGL patients who achieved remission than in patients who did not. The B12-associated factor may be an Ir gene. These results suggest that the tendency to develop AGL is influenced by one or more genes mapping in or near the HLA region. (23 refs.)

77-5205 **Histocompatibility Antigens in Adult Acute Leukemia.** (Eng.) Hester, J. P. (Dept. Developmental Therapeutics, Univ. Texas System Cancer Center, M. D. Anderson Hosp. and Tumor Inst., Houston, TX 77025); Rossen, R. D.; Templeton, J. W.; McCredie, K. B.; Freireich, E. J. *Prog Clin Biol Res* 16: 71-79; 1977.

The histocompatibility antigen (HLA) typing of 62 adult leukemia patients, their parents, and their siblings was compared with that of 150 normal unrelated Caucasian platelet donors. There was a statistically significant increased frequency of the A-locus specificity HLA-A11 in acute lymphoblastic leukemia (ALL) patients, parents, and siblings plus an increased frequency of A- and B-locus specificities HLA-AW19 and HLA-BW35 in the parents and siblings of ALL patients.

ALL patients did not differ significantly from either parents or siblings in A- or B-locus antigens. A slight but statistically insignificant increase in HLA-A11 was seen in acute myeloblastic leukemia (AML) patients, but there was no significant difference in the distribution of A-locus specificities among AML patients, their parents, and their siblings. B-locus antigen HLA-BW35 was elevated by 18% in AML patients, by 20% in their parents, and by 25% in their siblings. Based on these data, adult acute leukemia patients and their families apparently differ from normal controls with regard to HLA antigens. These differences are most apparent in ALL patients, who differ from AML patients in morphologic and cytochemical characteristics, frequency of incidence, and clinical course. (10 refs.)

77-5206 **HLA Antigens on Human Peripheral Lymphocytes and Spleen of Malignant Lymphoma and Other Cancer Patients.** (Eng) Cohen, E. (Dept. Breast Surgery, Roswell Park Memorial Inst., Buffalo, NY 14263); Kim, U.; Blumenson, L.; Gregory, S. G.; Khurana, U.; Cox, C. *Prog Clin Biol Res* 16: 181-186; 1977.

The HLA serological (individual reagent serum) discordance between human peripheral lymphocytes from the spleens of malignant lymphoma patients and those with other cancer was determined. The disease categories were (1) Hodgkin's disease; (2) lymphomas, lymphosarcomas, and chronic lymphocytic leukemia; (3) chronic myelocytic leukemia; and (4) others. Discordances of 6%-34% were noted. Regardless of differences in the frequency of serologic reactions that were detected between the cells of splenic origin rather than with the peripheral lymphocytes, the differences were not statistically significant. It was speculated that the 'extra' antigens that were detected by microcytotoxicity techniques may be due to artifacts of (1) multispecificity of sera, (2) populations of dead or injured cells, (3) non-HLA antigens detected by the particular reagent sera used, and (4) neoplasia-associated antigens, as yet undefined. (4 refs.)

77-5207 **Evaluation of Anomalous HLA Reactivity in the Typing of Neoplastic Lymphoreticular Cells.** (Eng) Huntington, S. J. (Div. Clinical Pathology, SUNY, Upstate Medical Center, Syracuse, NY 13210); Davey, F. R. *Prog Clin Biol Res* 16: 91-102; 1977.

An analysis of the anomalous major histocompatibility antigen (HLA) cytotoxic reactions observed on malignant lymphoid cells from 11 patients with acute lymphocytic leukemia (ALL; 6 cases) or non-Hodgkin's lymphocytic lymphoma (LL; 5 cases) revealed altered membrane markers on the neoplastic lymphoblasts. Lymphoblasts from the six ALL patients showed a paucity of receptors for T cells (E rosettes) and B cells (surface membrane immunoglobulin). In contrast, the neoplastic lymphoid cells from the five LL patients were determined to be B-cell proliferations in four and a T-cell tumor in the fifth. Anomalous HLA cytotoxic reactions were observed in all six cases of ALL, and probably in one of LL when lymphoblasts were used as target cells. The results suggest that some HLA antisera may be contaminated with a second antibody with specificity against non-T, non-B, leukemic lymphoblasts. The non-T, non-B lymphoblasts may contain a leukemia-associated antigen or some primitive lymphoid antigen. In mixed lymphocyte culture tests, there was no significant stimulation of normal peripheral blood autologous lymphocytes when they were incubated with neoplastic cells from any of ALL or LL patients. However, neoplastic lymphoid cells could stimulate allogeneic lymphocytes. (35 refs.)

77-5208 **The HLA System and Survival in Malignant Disease: Hodgkin's Disease and Carcinoma of the Breast.** (Eng) Falk, J. (Dept. Medicine and Surgery, Univ. Toronto, Toronto Western Hosp., Toronto, Ontario, Canada); Osoba, D. *Prog Clin Biol Res* 16: 205-216; 1977.

The relationship of major histocompatibility (HLA) antigens and survival in malignant disease was investigated. A prospective study of 79 patients with Hodgkin's disease revealed that patients lacking AW19 and/or B5 had a better prognosis for survival than those who had these antigens. In another study of 73 patients whose HLA phenotypes were determined after they had survived at least 5 yr, only B8 was significantly increased in frequency (37%) compared with disease-free controls (18%) and patients with recent onset of disease (19%). In a series of 207 patients with mammary carcinoma whose HLA antigens were identified soon after the onset of disease, there was no deviation from normal frequencies. However, in 185 patients with mammary carcinoma who had been followed for > 16 mo, the frequency of B8 in survivors (28.1%) was double that in nonsurvivors (14.0%). These results suggest that genes in the HLA region influence the survival of patients with these malignancies. The gene in the B region coding for B8 may be in nonrandom association with a gene(s) in the HLA complex that controls the magnitude of the response in the mixed leukocyte reaction. The association of other genes (eg, immune response genes) with genes in the A, B, C, and D regions of the HLA complex may contribute to survival in malignant disease by controlling factors other than antigenic specificity. (29 refs.)

77-5209 **Breast Cancer and HLA Relationship in a High-Risk Family.** (Eng) Rosner, D. (Dept. Breast Surgery, Roswell Park Memorial Inst., Buffalo, NY 14263); Cohen, E.; Gregory, S. G.; Khurana, U.; Cox, C. *Prog Clin Biol Res* 16: 169-174; 1977.

To study the possible role of the major histocompatibility (HLA) antigens in breast cancer, an investigation was made of HLA antigens and haplotypes in a high-risk family in which 5/8 sisters developed breast cancer, all during the premenopausal period (at ages 30-41). The cancer developed in the five older sisters. Five of the seven sisters who were tissue-typed carried the antigen HLA-B13, as did the mother (who died of ovarian carcinoma). The three younger sisters, two of whom carry HLA-B13, have cystic disease of the breast although they are still in their early twenties. This offers strong but inconclusive evidence of an association of HLA-B13 with a high-risk for breast cancer. (13 refs.)

77-5210 HLA in Breast Cancer-prone Families and the Cancer Family Syndrome. (Eng) Lynch, H. T. (Creighton Univ. Sch. Medicine, Omaha, NB 68178); Terasaki, P. I.; Guirgis, H. A.; Sherard, B. D.; Androsh, K. L.; Harris, R. E.; King, M. C.; Petrakis, N.; Lynch, J.; Maloney, K.; Rankin, L.; Lynch, P. M.; Elston, R.; Mulcahy, G.; Platt, R. *Prog Clin Biol Res* 16: 149-162; 1977.

In view of the possible relationship of the major human histocompatibility antigens (HLA) to nonmalignant and malignant diseases, data on HLA antigen and haplotype distribution in seven breast cancer-prone (BCP) families and in five families with the Cancer Family Syndrome (CFS) are presented. A total of 444/950 members of the BCP families were serotyped and/or retrohaplotyped. Overall, the frequencies of antigens B-15, A-24, A-28, A-29, B-35, and B-40 and haplotypes HL-A29-12, HL-A24-7, HL-A2-40, HL-A11-15, and HL-A2-7 were higher in these subjects than expected from nonfamilial data. Of particular interest was the occurrence of HL-A haplotype 29-12 in 5/7 BCP kindreds. For cancer patients of the BCP families, haplotypes HL-A29-12, HL-A1-8, HL-A2-40, and HL-A24-7 and antigens A-2, B-12, A-29, B-7, A-24, B-40, A-1, B-8, and A-11 were most prevalent. In the CFS families, with 418/3,498 members typed, there was no single haplotype that was observed consistently. Haplotypes HL-A1-8, HL-A2-12, HL-A3-35, HL-A24-40, and HL-A2-13 were the most prevalent in certain of the families, both overall and among cancer patients. An interesting finding was an excess frequency of cancer among double heterozygotes (36.2%) compared with single (10%) and double (16.7%) homozygotes. It is speculated that a more diverse array of HLA on the cell surface may result from a retrodifferentiation occurring conjointly with cell transformation. (17 refs.)

77-5211 Lack of Association Between Breast Cancer and HLA (A and B) Specificities: Importance of Age-matched Controls. (Eng) Oh, J. H. (Royal Victoria Hosp., McGill Univ., Montreal, Canada); MacLean, L. D. *Prog Clin Biol Res* 16: 163-167; 1977.

The distribution of the major histocompatibility (HLA) A and B antigens in 100 Caucasian breast cancer patients was compared with those in two different control groups. The first control group (I, 263 subjects) was age-unmatched (mean age 25 ± 3 yr), and the second control group (II, 75 subjects) was age-matched (53 ± 10 yr) to the patient group (56 ± 13 yr). Out of 23 HLA antigens compared, only 1, HLA-B13, was found to be significantly less prevalent among the patients compared with control Group I (1% vs 7.2%, $p = 0.025$ uncorrected). However, comparison between patients and control Group II showed no significant difference in the frequency of HLA-B13 (1% vs 1.3%, $p = 0.80$ uncorrected) or any other antigens. Thus, age is an important variable in studies of the correlation between HLA and disease. (10 refs.)

77-5212 HLA Antigens in Malignant Melanoma. (Eng) Bergholtz, B. (Tissue Typing Lab., National Hosp. Norway, Oslo, Norway); Brennhovd, I.; Klepp, O.; Kaakinen, A.; Thorsby, E. *Prog Clin Biol Res* 16: 175-180; 1977.

A possible association between the major histocompatibility (HLA) antigens and malignant melanoma was investigated by the HLA-A, -B, -C, and -D typing of 54 Norwegian melanoma patients and comparing the results with controls. For the first three types (A, B, C) there was a slight but not significant increase in the frequency of HLA-B27 among the melanoma patients. HLA-D typing by the mixed lymphocyte culture test demonstrated significant associations between certain determinants of the HLA-D and HLA-B series, indicating a linkage disequilibrium between some of the genes coding for these antigens. HLA-D determinant LD 108 showed the greatest deviation from normal frequency, being present in 21% of the patients but in only 8.6% of 209 healthy individuals. However, this deviation was not statistically significant. (15 refs.)

77-5213 HLA Antigens and Ia Antibody in the Gastric Cancer Patient. (Eng) Tsuji, K. (Blood and Tissue Typing Center, Dept. Surgery, Tokai Univ., Sch. Medicine, Bohseidai, Isehara, Kanagawa 259-11, Japan); Ito, M.; Inouye, H.; Nose, Y.; Hoshino, K.; Shibuya, K.; Tajima, T.; Mitomi, T. *Prog Clin Biol Res* 16: 29-37; 1977.

The major histocompatibility (HLA) antigenic phenotype, gene, and haplotype frequencies of 87 gastric cancer patients and 355 normal healthy Japanese were investigated for a possible association of HLA specificities with susceptibility to gastric cancer. Of 18 HLA specificities in the HLA-A locus and 23 specificities in the HLA-B locus examined, a significantly decreased frequency of HLA-B5 antigen was noted in gastric cancer patients (17.2%) compared with controls (40.0%). A9-B5 was the most frequent haplotype of controls, and A2-Blank B was most frequent in gastric cancer patients. Ia-like B-cell-specific antibody was detected in 2/20 gastric cancer patients studied, but no clear association between B-cell-specific antibody and clinical findings was noted. (21 refs.)

77-5214 **Chemical Properties of Human Ia Antigens.** (Eng.) Klareskog, L. (Inst. Medical and Physiological Chemistry, Biomedical Center and Blood Center, Univ. Hosp., Univ. Uppsala, Uppsala, Sweden); Sandberg-Tragardh, L.; Rask, L.; Lindblom, J. B.; Curman, B.; Peterson, P. A. *Nature* 265(5591): 248-251; 1977.

A cell membrane glycoprotein complex, controlled by the major histocompatibility complex HLA-D locus, was isolated from the leukemic cells of a patient with chronic lymphatic leukemia, and its antigenic characteristics were examined. Testing with HLA-D alloantiserum-induced cytotoxicity on the leukemia cells suggested that the HLA-D phenotype was Dw3 and Dw4. Cell surface proteins of the isolated cells were labeled by lactoperoxidase-catalyzed iodination, and Triton X-100-solubilized molecules reactive with the alloantisera directed against Dw3 and Dw4 determinants were precipitated and analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Both antisera precipitated two types of polypeptide chains with apparent mol wts of 28,000 and 34,000. Leukemic cells were cultured in the presence of ^{3}H-leucine and ^{3}H-fucose, and radiolabeled molecules reactive with alloantisera against Dw3 and Dw4 determinants were isolated and analyzed by electrophoresis. With either of the radioactive labels, the two-polypeptide-chain pattern was evident, indicating that both chains contain carbohydrate moieties. In the absence of reducing conditions, the two polypeptide chains were separated and, therefore, no covalent interaction was apparent. A rabbit antiserum raised against the protein complex did not cross react with HLA antigens derived from the A, B, and C loci. Neither did heteroantisera directed against the A, B, and C loci gene products react with the glycoprotein complex. This suggests that there is no apparent immunological similarity between the molecules coded for by the D locus and those coded for by the A, B, and C loci. These data strongly suggest that the HLA-D locus controls the expression of polypeptide chains that are the equivalents of the murine Ia antigens. (17 refs.)

77-5215 **Fetal Antigen Modulation in Chemical and Viral Transformed Cells (MeetingAbstract).** (Eng) Evans, D. L. (Bowman Gray Sch. Medicine, Winston-Salem, NC 27103); Parker, D. V. *In Vitro* 13(3): 171; 1977. (no refs.)

77-5216 **Role of Fetal Antigens in Tumor Immunity.** (Eng.) Gautam, S. (Div. Surgical Sciences, Section Transplantation Biology, Clinical Res. Centre, Watford Road, Harrow, HA1 3UJ Middlesex, England); Aikat, B. K. *Eur J Cancer* 13(1): 71-79; 1977.

Injection of viable fetal cells into inbred C57 (jet black, ICRC) mice followed by challenge with transplanted 3-methylcholanthrene-induced tumor cells after 7, 14, and 21 days significantly delayed the time of tumor appearance. Transfer of lymphoid cells from immunized mice had the same effect. Injection of viable tumor cells pretreated in vitro with serum from mice immunized with fetal cells shortened the time of tumor appearance. (32 refs.)

77-5217 **Electron Microscopy of the HBsAg from Human Hepatoma Cell Line (Letter to Editor).** (Eng.) Stannard, L. M. (M.R.C. Virus Res. Unit, Univ. Cape Town, Observatory, Cape 7925, South Africa); Alexander, J. *Lancet* 2(8040): 713-714; 1977.

Electron microscopy of the tissue culture fluid of a primary hepatoma line from a patient with circulating hepatitis B surface antigen (HBsAg) revealed tubular and spherical HBsAg components identical with those in the sera of HBAg carriers. Five antisera without HBsAg all produced HBsAg immune complexes when mixed with the culture fluid. This cell line could be valuable in studying the pathogenesis of serum hepatitis and the morphogenesis of HBAg. (4 refs.)

77-5218 **Antigenic Heterogeneity within Primary 3-Methylcholanthrene-induced Rat Sarcomas (Meeting Abstract).** (Eng.) Pimm, M. V. (Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham, England). *Br J Cancer* 36(3): 414; 1977. (1 ref.)

77-5219 **A Putatively New Antigen (CSAp) Associated with Gastrointestinal and Ovarian Neoplasia.** (Eng.) Pant, K. D. (Div. Experimental Pathology, Dept. Pathology, Univ. Kentucky Coll. Medicine, Lexington, KY 40506); Dahlman, H. L.; Goldenberg, D. M. *Immunol Commun* 6(4): 411-421; 1977.

Colon-specific antigen-p (CSAp), which appears to be almost exclusively restricted to human intestinal tissues and which is quantitatively increased in gastrointestinal neoplasms, is described. First identified in GW-39 human colonic carcinomas serially grafted in hamsters, CSAp was found in gastric and colonic carcinomas, ovarian mucinous cystadenocarcinomas, colonic polyps, some benign ovarian tumors, fetal colon and small intestine, and normal adult small and large intestines. Morphologically normal colon adjacent to colon cancer also contained increased levels of CSAp. Hemagglutination-inhibition assay revealed only trace amounts of CSAp in the esophagus, stomach, pancreas, and liver, and the antigen was totally absent from other normal and malignant tissues, such as the lung, kidney, breast, cervix, skin, and bone. Gel immunodiffusion patterns showed that CSAp is immunologically distinct from carcinoembryonic antigen, nonspecific cross-reacting antigen, α-fetoprotein, beta oncofetal antigen, and human liver ferritin. CSAp appears to be a possibly new fetal substance with a high degree of specificity for gastric, colonic, and ovarian tissues. (14 refs.)

77-5220 **Immunological Studies of Induced Tumors of the Rat Submandibular Gland.** (Eng.) El-Mofty, S. (28 Abd El-Azim Rashed St., Agouza, Cairo, Egypt). *Oncology* 34(2): 53-57; 1977.

Changes in tissue-specific antigens and the appearance of new antigenic components in malignantly transformed rat submandibular glands were studied. Submandibular gland carcinoma was induced in inbred 4-mo-old male Fischer rats by 9,10-dimethyl-1,2-benzanthracene (DMBA), and the resulting antigenic activities were evaluated using rabbit antisera to both normal submandibular gland extract and extracts of the induced tumors. The concentration of several normally intrinsic antigens was lower in all tumors and premalignant lesions. Although all the tumors were well-differentiated epidermoid carcinomas, there was considerable antigenic variation among individual tumors. The number of precipitin bands ranged from three to five, and each tumor yielded bands corresponding to α- and β-globulins. The remaining bands differed from one tumor to another. Since the morphology and biological behavior of DMBA-induced submandibular tumors in rats have been shown to be similar to human oral carcinoma, these tumors might provide a useful model system for the further study of oral carcinoma. (34 refs.)

77-5221 **Studies on Circulating Immune Complexes in Mice with Growing Methylcholanthrene Induced Fibrosarcomas (MCAF) (Meeting Abstract).** (Eng.) Platzer, E. (Inst. Clinical Immunology, Erlangen, W. Germany); Warnatz, H. *Z Immunitaetsforsch* 153(4): 342; 1977. (1 ref.)

77-5222 **Characterization of Effector Lymphocytes Associated with Immunity to Murine Sarcoma Virus (MSV)-induced Tumors. II. Repeated Stimulation and Proliferation In Vitro of Specific Cytolytic T Lymphocytes.** (Eng.) Plata, F. (Laboratoire d'Immunologie et de Virologie des Tumeurs INSERM U 152, Hopital Cochin, 75014 Paris, France); Jongeneel, C. V. *J Immunol* 119(2): 623-629; 1977.

Experiments were designed to study cytolytic T lymphocyte (CTL) generation from C57BL/6 murine sarcoma virus (MSV)-immune spleen cells upon repeated stimulation in vitro with irradiated, syngeneic RBL-5 lymphoma cells. Although CTL activity in secondary mixed leukocyte tumor cell (sec-MLTC) cultures drastically decreased between days 7 and 16, tertiary stimulation with irradiated RBL-5 cells regenerated 4.5 x 10^5 active CTL per 10^6 cells. Tertiary stimulation with syngeneic C57BL/6 normal spleen cells had little effect. Quaternary stimulation of tertiary MLTC (ter-MLTC) with irradiated RBL-5 cells yielded 5 x 10^5 active CTL per 10^6 cells. Dose-response studies showed that less tumor antigen was necessary in sec-MLTC than in ter-MLTC for optimal CTL generation. Optimum results were obtained at a ratio of 20 lymphocytes to 1 stimulating cell in sec-MLTC and at 5:1 in ter-MLTC. This may indicate a difference in the nature and/or relative frequencies of CTL precursor cells in MSV-immune spleen and in long term sec-MLTC. This difference is also suggested by the fact that net CTL generation was also detectable in ter-MLTC at ratios of 1,000:1 and 1:1, but not in sec-MLTC. Since only syngeneic tumor cells bearing MSV-associated antigens were able to induce high levels of CTL regeneration in ter-MLTC, the tumor antigen used for the initial stimulation of MSV-immune spleen cells in sec-MLTC also appears to have induced a specific selection of CTL precursor cells. Evidence is thus provided for the existence of fundamental similarities between CTL responses to major histocompatibility alloantigens in MLC and CTL responses to MSV-associated tumor antigens in syngeneic MLTC. (38 refs.)

77-5223 **Dissociation of Effector Functions in Populations of Activated Macrophages.** (Eng) Wing, E. J. (Div. Infectious Diseases, Dept. Medicine, Stanford Univ. Sch. Medicine, Stanford, CA 94305); Gardner, I. D.; Ryning, F. W.; Remington, J. S. *Nature* 268(5621): 642-644; 1977.

This study demonstrates that activated macrophages characterized by one functional criterion do not necessarily possess other functional characteristics of activated macrophages and that differences in functional capacity depend on the activation method. Macrophages were activated by three methods: (I) *Trichinella spiralis* infection in C57B1/6 mice, (II) C37 strain *Toxoplasma gondii* infection in BALB/c mice, and (III) C56 strain *T. gondii* infection in Swiss Webster mice. Macrophages from the peritoneal exudates of I and II could inhibit tumor cell DNA synthesis, but they were unable to prevent intracellular multiplication of *T. gondii*. Macrophages from III challenged immediately after isolation inhibited DNA synthesis by the tumor cells and intracellular multiplication of *T. gondii*. Incubation of macrophages from III in vitro for 24 hr resulted in a loss of capacity to inhibit tumor cell DNA synthesis, but the capacity to inhibit intracellular multiplication of *T. gondii* was retained. Whether there are subpopulations of macrophages that become activated for different functions or all macrophages are activated differentially for different functions remains unknown. (20 refs.)

77-5224 **Arming of Macrophages with Lymphocytes from Mice Immunized with Tumor Tissue.** (Eng.) Horowitz, M. (Dept. Microbiology, Sch. Medicine, State Univ. New York, Upstate Medical Center, Syracuse, NY 13210); Argyris, B. F. *Immunol Commun* 6(3): 297-319; 1977.

The role of B and T cells in the arming of macrophages was investigated. C57BL/6 mouse macrophages were rendered specifically cytotoxic ("armed") by incubation with spleen cells from C57BL/6 mice sensitized in vivo with allogeneic P-815 mastocytoma cells. By determining the number of lymphocytes adhering to armed macrophages and analyzing the quantitative aspects of the arming process, it was concluded that the cytotoxicity of armed macrophages is not due to the presence of contaminating lymphocytes. Tumor-sensitized spleen cells were separated into T- and B-cell-enriched subpopulations that were tested separately for their ability to arm macrophages. The results suggest that B cells contribute little or nothing to the arming process. The arming ability of proliferating T lymphocytes and cytotoxic T lymphocytes was compared in several systems. The results indicate that the cytotoxic T cell seems to be the cell responsible for the arming of macrophages. (31 refs.)

77-5225 **The Molecular and Cell-surface Changes Associated with Morphological Alterations Mediated by Dibutyryladenosine 3:5-Cyclic Monophosphate in Rat Cells.** (Eng.) Rieber, M. (Centre Microbiology and Cell Biology, Instituto Venezolano de Investigaciones Cientificas, Apartado 1827, Caracas, Venezuela); Meza, A. T. *Biochem Soc Trans* 5(4): 1140-1141; 1977.

The *ts*-NT3-KR cell line (a cloned derivative of normal rat kidney cells transformed by the temperature-sensitive *ts* 339 derivative of B77 virus) was used to determine that the similar morphological effect of dibutyryl cyclic AMP on cells grown at 37 C or 33 C leads to different cell-surface alterations. Anti-(concanavalin A) serum had a differential cytolytic effect in the presence of complement. (5 refs.)

77-5226 **Lymphoid Cells and Mouse Mammary Tumorigenesis: A Subpopulation of Lymphocytes Responding to Con A and PHA Mitogens and Possessing Fc Receptors (Meeting Abstract).** (Eng.) Epstein, R. S. (Univ. Miami Sch. Medicine, Miami, FL); Lopez, D. M.; Sigel, M. M. *Clin Res* 25(4): 641A; 1977. (no refs.)

77-5227 **Studies of the Protective Role of Lymphoid Cell Populations in Tumors Caused by the Avian Reticuloendotheliosis Virus (Strain T) (Meeting Abstract).** (Eng.) Pasternak, R. D. (Temple Univ., Philadelphia, PA 19122). *Diss Abstr Int [B]* 38(4): 1645; 1977. (no refs.)

77-5228 **Antiviral T Cell-mediated Immunity in Marek's Disease.** (Eng) Ross, L. J. (Houghton Poultry Res. Station, Houghton, Huntington, Cambridgeshire, England). *Nature* 268(5621): 644-646; 1977.

Sensitized lymphocytes obtained from White Leghorn chickens immunized with Marek's disease virus (MDV) reacted against MDV-specific antigens in a plaque inhibition assay. The effector cells were characterized as T lymphocytes by the use of anti-T and anti-B sera with complement. The T cells acted independently (one-hit kinetics) to inhibit plaque formation, probably by a direct lethal interaction between sensitized cells and MDV-infected target cells. Hitherto unrecognized virus-specific antigens present at the surface of infected WBC may act as targets for sensitized lymphocytes. It is possible that the T cells operate in vivo to eliminate infected WBC and the spread of MDV throughout the tissues of infected birds. (12 refs.)

77-5229 **Cell-mediated Immune Responses in Patients with Recurrent Herpes Simplex Infections. II. Infection-associated Deficiency of Lymphokine Production in Patients with Recurrent Herpes Labialis or Herpes Progenitalis.** (Eng.) O'Reilly, R. J. (Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021); Chibbaro, A.; Anger, E.; Lopez, C. *J Immunol* 118(3): 1095-1102; 1977.

Lymphocyte transformation and production of leukocyte migration inhibitory factor were examined in 34 patients with recurrent and 8 with previous non-recurrent herpes simplex infection, and in 17 normal controls. Patients with a high frequency of infections were able to mount cell-mediated responses to the virus which differed from lymphoproliferative responses seen in controls. (31 refs.)

77-5230 **Inhibition of In Vitro Lymphoproliferative Responses by In Vivo Passaged Rat 13762 Mam-**

mary Adenocarcinoma Cells. I. Charateristics of Inhibition and Evidence for an Infectious Agent. (Eng) Campbell, D. A. (Lab. Immunodiagnosis, NCI, Building 10, Room 8B11, Bethesda, MD 20014); Manders, E. K.; Oehler, J. R.; Bonnard, G. D.; Oldham, R. K.; Herberman, R. B. *Cell Immunol* 33(2): 364-377; 1977.

When added as third-party cells to mitogen response assays or mixed lymphocyte cultures, small numbers of x-ray inactivated 13762 mammary adenocarcinoma cells caused a significant reduction in the viability of the cocultivated lymphocytes and completely inhibited the expected lymphoproliferative responses. The factor(s) apparently responsible for the inhibitory effect was preserved after ultrasonic disruption of the tumor cells, could be sedimented by ultracentrifugation, and was sensitive to UV light. In addition, the cytopathic effects were serially propagated using cell-free supernatants obtained from sonicated 13762 tumor cells. These results suggest that the 13762 adenocarcinoma line, as carried in vivo in Fischer rats, harbors an infectious particle that can affect the proliferative responses of lymphocytes in vitro. (38 refs.)

77-5231 **Cell Lines from Angio-immunoblastic Lymphadenopathies (AIL) and Immunoblastic Sarcomas (IS) (Meeting Abstract).** (Eng.) Yerganian, G. (Sidney Farber Cancer Institute, Boston, MA 02115); Paika, I. J.; Penta, A.; Liu, T.; Nell, M. A. *In Vitro* 13(3):175; 1977. (no refs.)

77-5232 **Characterization of a Carcinogen-induced Murine B Lymphocyte Cell Line of C3H/eB Origin.** (Eng.) Bergman, Y. (Dept. Chemical Immunology, Weizmann Inst. Science, Rehovot, Israel); Haimovich, J. *Eur J Immunol* 7(7): 413-417; 1977.

Tumor cells possessing IgM (membrane immunoglobulins) were found in a carcinogen-induced tumor (38C-13) from a T-cell-depleted C3H/eB mouse. The cells of this tumor were adapted to continuous culture in vitro and characterized with respect to their cell-surface components The cells possess IgM on their surface but do not secrete it. This IgM is composed of μ and light chains with mol wts similar to those of an IgM myeloma protein. Isoelectric focusing revealed that the IgM is homogeneous. The cells possess Fc receptors, but they lack C receptors and Ia antigens. The characteristics of the cell-surface components of 38C-13 cells indicate that they belong to a particular B-cell clone at an early stage of differentiation. (42 refs.)

77-5233 **Membrane Receptor Stripping Confirms the Association Between EBV Receptors and Complement Receptors on the Surface of Human B Lymphoma Lines.** (Eng.) Yefenof, E. (Dept. Tumor Biology, Karolinska Inst., S 104 01 Stockholm 60, Sweden); Klein, G. *Int J Cancer* 20(3): 347-352; 1977.

To determine whether there is a relationship between Epstein-Barr virus (EBV) receptors and complement (C3) receptors on human B lymphoma cells, the binding of infectious virus particles to EBV receptors was measured by quantitative assay of the residual supernatant for infectivity. Ramos and BJAB, two EBV-negative B lymphoma cell lines derived from an American Burkitt's lymphoma and an African Burkitt-like lymphoma, respectively, were used for stripping and EBV absorption. Raji, an EBV-carrying nonproducer cell line from an African Burkitt's lymphoma, was used as a target for infection by EBV. Stripping the membranes of EBV receptors or C3 receptors eliminated or significantly reduced the cells' ability to absorb infectious EBV. However, stripping of the Fc receptors, membrane IgM and beta$_2$ microglobulin did not reduce EBV absorption. This shows that the EBV receptor of the B lymphocyte is structurally related to the C3 receptor. (14 refs.)

77-5234 **Induction of Plaque-forming Cells in Cultured Human Lymphocytes by Combined Action of Antigen and EB Virus.** (Eng.) Luzzati, A. L. (Basel Inst. for Immunology, 487 Grenzacherstrasse, Postfach 4005 Basel 5, Switzerland); Hengartner, H.; Schreier, M. H. *Nature* 269(5627): 419-420; 1977.

An attempt was made to induce a specific antibody response in human peripheral blood lymphocytes using Epstein-Barr virus and sheep RBC. This combination consistently produced an anti-sheep RBC response. Whether the virus acts directly on B cells or through induction of helper T cells to evoke this response is currently being investigated. (13 refs.)

77-5235 **EB Virus-induced B Lymphocyte Cell Lines Producing Specific Antibody.** (Eng.) Steinitz, M. (Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm 60, Sweden); Klein, G.; Koskimies, S.; Makel, O. *Nature* 269(5627): 420-422; 1977.

Studies of immortalization of human B lymphocytes by Epstein-Barr virus resulted in the establishment of cell lines carrying a specific surface receptor and secreting the corresponding antibody. It should thus be possible to manufacture B cell lines for the production of particularly interesting antibodies. (15 refs.)

77-5236 **Antitumor Antibodies in Human Breast Cancer Sera as Detected by Fixed Cell Immunofluores-**

cence and Living Cell Membrane Immunofluorescence Assays. (Eng.) Nordquist, R. E. (Cancer Res. Program, Oklahoma Medical Res. Foundation, 825 N.E. 13th St., Oklahoma City, OK 73104); Schafer, F. B.; Manning, N. E.; Ishmael, D. R.; Hoge, A. F. *J Lab Clin Med* 89(2): 257-261; 1977.

Fixed cell immunofluorescence and living cell membrane immunofluorescence tests were used to study the reactivity of cells from patients with breast carcinoma, breast fibroadenoma, and cystic mastitis against a cultured human breast cancer cell line. A significant humoral immune response was observed that appeared to cross-react with breast tumors of the same histological type in other patients. (8 refs.)

77-5237 **Fine Specificity of Rabbit Anti-p-azophenylphosphorylcholine Antibodies; Comparison with HOPC-8 Myeloma Protein.** (Eng.) Krausz, L. M. (Dept. Immunology Res., Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263) Grossberg, A. L.; Pressman, D. *Immunochemistry* 13(11): 901-905; 1977.

To study the binding site of rabbit antibodies raised against the p-azophenylphosphorylcholine (APPC) group and the phosphorylcholine binding site of mouse myeloma protein HOPC-8, the relative binding constants of several choline-related small molecules with anti-APPC antibodies and with HOPC-8 were measured. Anti-APPC antibody sites had a lower degree of cross reactivity for substructures of the APPC group than did the HOPC-8 site. The most important structure for binding to both kinds of sites was the positively charged quaternary ammonium group, indicating a close approach of this group to a negatively charged carboxylate present in both sites. The negatively charged phosphoryl group appeared more important for binding to the HOPC-8 site than to the anti-APPC site, indicating that this structure probably more closely approaches the positively charged guanidinium group present in the HOPC-8 site than it does a similar group present in the anti-APPC site. (13 refs.)

77-5238 **Natural Autoantibodies Cytotoxic for Thymus Cells and for Neuraminidase-treated Leukemia Cells in the Sera of Normal AKR Mice.** (Eng.) Schlesinger, M. (Dept. Experimental Medicine and Cancer Res., Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel); Bekesi, J. G. *J Natl Cancer Inst* 59(3): 945-950; 1977.

The sera of normal inbred female AKR mice (2-3 mo of age) contained two types of naturally occurring autoantibodies. Heat-labile IgM autoantibodies were cytotoxic for syngeneic and allogeneic mouse thymus cells in the presence of guinea pig complement, but not for lymph node or spleen cells. Absorption experiments indicated that although its concentration was eight times higher on thymus cells than on other types of lymphoid cells, the antigen with which these antibodies react was present in all examined tissues of AKR mice. D-mannose (1.25-2.5 milliM), α-methyl-D-mannopyranoside (0.6-1.2 milliM), and L-fucose (0.6-2.5 milliM) each inhibited the cytotoxicity of normal AKR sera toward thymus cells. The other type of antibody reacted with neuraminidase-treated AKR leukemia cells, and it was also IgM in nature, heat-labile, absorbed by various murine tissues, and inhibited by D-galactose (38-75 milliM), lactose (38-75 milliM), L-fucose (150 milliM), and α-methyl-D-mannopyranoside (75 milliM). (39 refs.)

77-5239 **Seroepidemiologic Studies on the Possible Relationships of Human and Bovine Leukemia: Brief Communication.** (Eng.) Donham, K. J. (Comparative Medicine Section, Inst. Agricultural Medicine and Environmental Health, Coll. Medicine, Univ. Iowa, Oakdale, IA 52319); VanDerMaaten, M. J.; Miller, J. M.; Kruse, B. C.; Rubino, M. J. *J Natl Cancer Inst* 59(3): 851-853; 1977.

A seroepidemiologic study was conducted in search of antibodies to bovine leukemia virus (BLV) in people exposed to cattle with lymphosarcoma. Twenty-one dairy herds with documented cases of lymphosarcoma were identified, and sera from 282/846 cows from these herds were serologically positive. No positive sera were found in 45 dairy farmers, their relatives, and farm employees associated with these herds. Consumption of raw milk was reported by 77% of the farm group. Sera from 83 veterinarians, 30 leukemia patients, and 200 human controls were also negative for antibodies to BLV. (19 refs.)

77-5240 **Restricted Heterogeneity of Antibodies to Idiotypes of Isologous Immunoglobulins.** (Eng.) Sakato, N. (Res. Inst. Microbial Diseases, Osaka Univ., Yamada-Kami, Suita-Shi, Osaka, Japan); Hall, S. H.; Eisen, H. N. *Immunochemistry* 14(8): 621-625; 1977.

The heterogeneity of isologous anti-idiotypic antibodies was studied by examining antibodies raised in BALB/c mice against the M167 myeloma protein (an IgA myeloma protein of BALB/c origin). The anti-idiotypic antibodies were predominately IgGl. Their heterogeneity with respect to affinity and isoelectric point was highly restricted. Since the immunization procedure used tends to evoke highly heterogenous antibody responses, these antibodies thus appear to be notably homogeneous. (26 refs.)

77-5241 **Uncommon Gm Phenotypes in Sera from Neuroblastoma Patients.** (Eng.) Morell, A. (Inst.

Clinical and Experimental Cancer Res., Univ. Berne, Tiefenau-Hosp., 3004 Berne, Switzerland); Kaser, H.; Scherz, R.; Skvaril, F. *J Immunol* 118(3): 1083-1085; 1977.

Studies on the sera from 68 neuroblastoma patients revealed a high frequency of the uncommon Gm phenotypes Gm (a+, f+, g-, b+) and Gm (a+, f+, g+, b-) as compared with normal blood donors. In two of the nine cases of Gm abnormality, the gene complexes coding for the unusual Gm phenotype were traced to the mother. All nine cases were without IgG subclass abnormalities in the sera. (22 refs.)

77-5242 **Initiation and Translation In Vitro of mRNA for MOPC 315 Immunoglobulin Heavy Chain and Characterization of Translation Product.** (Eng.) Bedard, D. L. (Dept. Biology, Johns Hopkins Univ., Baltimore, MD 21218); Huang, R. C. *J Biol Chem* 252(8): 2592-2598; 1977.

Studies were conducted to determine whether there is an NH_2-terminal precursor for mineral oil-induced plasmacytoma 315 heavy-chain immunoglobulin (H^{315}) and to judge the accuracy of translation and extent of elongation of H^{315} messenger RNA (mRNA) in a crude rabbit reticulocyte lysate system. Results strongly indicate the fidelity of initiation and elongation of H^{315} in the lysate. (35 refs.)

77-5243 **The Occurrence of Polyclonal Immunoglobulin G in Hodgkin's Disease and Relationship to Pathogenesis.** (Fre.) Sandor, G. (Institut Pasteur, 25, rue du Docteur-Roux, 75015 Paris, France). *CR Acad Sc [D] (Paris)* 284(24): 2585-2587; 1977.

A determination of serum proteins in 29 patients with Hodgkin's disease (16 untreated) showed that over one-half of the patients had type V IgG. However, the IgG level was lower than normal in two-thirds of the treated patients. The difference between treated and untreated patients was statistically significant ($p < 0.01$). The IgG levels in the untreated patients were similar to those in patients with different collagenous diseases. It is concluded that Hodgkin's disease appears to be an autoimmune, anti-T-lymphocyte disease. (15 refs.)

See also:

* (Rev.): 77-4812, 77-4840, 77-4847, 77-4850, 77-4851, 77-4852, 77-4853, 77-4854, 77-4855.
* (Chem.): 77-4894, 77-4895.
* (Phys.): 77-5021, 77-5022.
* (Viral): 77-5055, 77-5076, 77-5079, 77-5082, 77-5086, 77-5099, 77-5105, 77-5117, 77-5129, 77-5130, 77-5131, 77-5136, 77-5149, 77-5151, 77-5152, 77-5159, 77-5160, 77-5174.
* (Path.): 77-5249, 77-5254, 77-5264, 77-5296, 77-5303, 77-5305, 77-5307, 77-5308, 77-5316.
* (Epid.-Biom.): 77-5336, 77-5359.

PATHOGENESIS

77-5244 **Cytoplasmic Microtubules in Transformed Mouse x Nontransformed Human Cell Hybrids: Correlation with In Vitro Growth.** (Eng) Miller, C. L. (Program in Biophysical Cytology, Dept. Biology, Univ. Pennsylvania, Philadelphia, PA 19104); Fuseler, J. W.; Brinkley, B. R. *Cell* 12(1): 319-331; 1977.

Patterns of cytoplasmic microtubules in somatic cell hybrids between transformed mouse cells and nontransformed human skin fibroblasts were examined using antitubulin antibodies as immunofluorescent probes. Nontransformed cells exhibit an extensive cytoplasmic microtubule complex (CMTC); in transformed cells, this complex is greatly diminished. Hybrid populations contained both types of cells. In addition, they contained cells with previously undescribed intermediate CMTC phenotypes. The percentage of each phenotype in hybrid populations was determined for 16 hybrid clones. Seven clones were found that appeared transformed on the basis of their CMTC pattern. The others comprised various proportions of all the cell types described. Repeated quantitation of the proportions of these types in the hybrid populations showed them to be stable with time in culture. In vitro growth of the hybrid clones was assayed by determining their saturation densities, plating efficiencies on plastic and colony-forming abilities in soft agar. This growth was directly proportional to the percentage of cells that showed the greatly diminished CMTC pattern. This indicates that a greatly reduced CMTC is associated with transformed behavior, especially the increased capacity of transformed cells for in vitro growth. (30 refs.)

77-5245 **Vascular Volume and Perfusion in Hamster Cheek Pouch Carcinomas and Tumor-bearing Cheek Pouches.** (Eng) Lurie, A. G. (Dept. Oral Radiology, Univ. Connecticut Health Center Sch. Dental Medicine, Farmington, CT 06032); Nintzel, B. B.; Rippey, R. M. *Cancer Res* 37(10): 3484-3489; 1977.

Changes in blood volume and perfusion in 7,12-dimethylbenz(a)anthracene (DMBA)-induced hamster cheek pouch carcinomas, tumor-bearing pouch tissue, and normal pouch tissue were studied by distribution of ^{51}Cr-labeled RBC and ^{86}RbCl. Squamous cell carcinomas were induced in male Syrian golden hamsters by repeated topical applications of 0.5% DMBA in mineral oil. Normal and tumor-bearing hamsters received iv injections of 20 μCi ^{51}Cr-labeled hamster RBC, followed in 10 min by 50 μCi ^{86}RbCl. Pouches and tumors were everted, clamped separately, and excised separately 90 sec after ^{86}RbCl injection, and the tumor vols were determined. Radioactivity was determined by scintillation spectrometry, and histopathological evaluations were also performed. Tumor ^{51}Cr and ^{56}Rb activities were less than those of control pouches in small tumors (vol < 10 mm^3), and then rose steadily thereafter to levels above those of control pouches but less than those of tumor-bearing pouches. Tumors with vol > 10 mm^3 were squamous cell carcinomas except for one papilloma. Statistical analysis of the tumor isotopic distribution values showed correlation between tumor hemodynamic changes and tumor vol and histopathology. Histopathologically defined malignant changes and increasing tumor sizes were accompanied by increasing tumor volume and blood perfusion. Increases in blood vol and perfusion also occurred in tumor-bearing pouch tissue. These results support the concept of the relation of rapid tumor growth and malignant behavior to tumor neovascularization, initiated possibly by a chemical mediator such as tumor angiogenesis factor. (35 refs.)

77-5246 **Metastasis Results from Preexisting Variant Cells Within a Malignant Tumor.** (Eng.) Fidler, I. J. (Basic Res. Program, NCI Frederick Cancer Res. Center, Frederick, MD 21701); Kripke, M. L. *Science* 198(4306): 893-895; 1977.

The heterogeneity of parental murine melanoma tumors was examined. A suspension of transplantable B16 melanoma parent line cells was divided into two parts. One portion was given to syngeneic C57BL/6 mice (5 x 10^4 viable cells in 0.2 ml, iv) and the other was used to produce single cell clones via a soft agarose-microculture technique and then injected iv into C57BL/6 mice. The number of pulmonary nodules per mouse obtained with the parent B16 line ranged from 8 to 131 (median 40.5). The number of pulmonary nodules and, thus, the metastatic potential of each of the single cell clones differed dramatically, varying from 0 to 15 nodules per mouse to 160 to 450 per mouse. There was also considerable variation among the clones in the number and sites of extrapulmonary metastases. Only 2/17 clones tested were statistically indistinguishable from the parent line. To determine whether the observed variability might have been introduced by cloning rather than by parental heterogeneity, subclones were produced. No statistically significant variability was seen in the nodules produced by these latter subclones. These results suggest that the parent B16 tumor was extremely heterogeneous with respect to the metastatic potential of its individual cells. They also support the suggestion that tumor cell variants arise in vivo within developing tumors, are subjected to host selection pressures, and are responsible for the emergence of new sublines with increased malignant potential. (9 refs.)

77-5247 **Chromosomes and Causation of Human Cancer and Leukemia. XXII. Karyotypic Changes in Malignant Melanoma.** (Eng) Kakati, S. (Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263); Song, S. Y.; Sandberg, A. A. *Cancer* 40(3): 1173-1181; 1977.

Karyotypic studies were performed on malignant melanoma cells from four men, aged 50, 61, 73, and 55 yr. The modal number in two cases varied from 39 to 43 (hypodiploid) with 5 to 13 marker chromosomes. The other tumors had modal numbers ranging from 63 to 157 (polyploid) with 11 to 40 marker chromosomes. The chromosome most involved in aberrations was number 1, with a total of 11 breakpoints in three of these patients. The most common breakpoints were 1q21, 1q25, and 1q32. Contrary to findings with some of the other chromosomes, however, the centromeric region of chromosome number 1 was not involved in the breaks. Although there were no common markers among these patients, common markers in various other tumors have been noted. (31 refs.)

77-5248 **Juvenile Melanoma--A Case Report and Histogenetic Investigation.** (Eng.) Niizuma, K. (Dept. Dermatology, Tokai Univ. Sch. Medicine, Bohseidai, Isehara, Kanagawa, 259-11 Japan). *Arch Dermatol Res* 259(1): 83-89; 1977.

A benign melanoma that appeared to be completely intradermal, occurring in a 15-mo-old girl, was investigated by light and electron microscopy. Results suggest that the tumor was composed exclusively of melanogenic nevus cells and that involvement of Schwannian nevoblasts could be excluded. This supports the concept that the melanoblastic nevoblasts derive solely from abnormal neural crest cells. (14 refs.)

77-5249 **Quantitation and Immunocytochemical Localization of Human Skin Collagenase in Basal Cell Carcinoma.** (Eng) Bauer, E. A. (Div. Dermatology, Washington Univ. Sch. Medicine, St. Louis, MO 63110); Gordon, J. M.; Reddick, M. E.; Eisen, A. Z. *J Invest Dermatol* 69(4): 363-367; 1977.

Human skin collagenase was quantitated by radioimmunoassay in 21 basal cell carcinomas. Immunoreactive collagenase protein was approx twofold greater in the tumor extracts than in normal skin extracts, suggesting that this enzyme may be important in the pathogenesis of soft tissue destruction in vivo. To further define the role of collagenase in such destruction, immunofluorescent staining with specific antiserum to human skin collagenase was used to localize collagenase in the basal cell carcinomas. The enzyme was found only in the stromal elements surrounding the tumor islands. No staining of the epithelial components of the basal cell carcinoma was observed. These findings suggest that the normal connective tissue elements may have been stimulated to produce an increased amount of collagenase, and they emphasize the importance of epithelial-stromal interaction in soft tissue invasiveness. (40 refs.)

77-5250 **Ultrastructure of Elastofibroma.** (Eng) Akhtar, M. (Dept. Pathology, Univ. Texas Medical Sch. at Houston, 6400 W. Cullen St., Houston, TX 77030); Miller, R. M. *Cancer* 40(2): 728-735; 1977.

An elastofibroma from a 69-yr-old man was examined by light and electron microscopy to study its morphogenesis. The lesion was comprised of abundant collagen fibers and numerous randomly disposed masses of amorphous elastinophilic material. These structures arose within aggregates of dense fibrillar material in the form of amorphous zones that merged with one another. The dense fibrillary material appeared to be produced by the fibroblasts and was comprised of fine fibrils embedded in a matrix of markedly dense ground substance. Incorporation of collagen fibers within the young elastic masses was also a frequent finding. Some of these masses contained central cores that resembled normal mature elastic tissue. These findings demonstrate that the abnormal elastic material in elastofibroma is derived from excessive production of young elastic tissue that shows a marked retardation of maturation. Most of the fibroblasts manifested morphologic evidence of active synthesis and release of collagen and also showed prominent nuclear fibrous laminae. This is consistent with the concept of a possible relationship between the functional status of a cell and the prominence of its fibrous lamina. (12 refs.)

77-5251 **The Ultrastructure of Malignant Fibrous Histiocytoma (Case Report).** (Eng) Lombardi, L. (Div. Experimental Oncology A, Instituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy); Pilotti, S.; Carbone, A.; Rilke, F. *Tumori* 63(4): 387-396; 1977.

A malignant fibrous histiocytoma of the soft tissue was studied by light and electron microscopy. The presence of fibroblast-like cells, histiocyte-like cells, undifferentiated stem cells, and xanthomatous cells was confirmed. The occurrence of lysosomes in some fibroblast like cells, the features of the undifferentiated stem cells, and the presence of cells with intermediate characteristics common to xanthomatous, histiocytic, and stem cells suggest that the various tumor cells all originated from tissue histiocytes. (11 refs.)

77-5252 **Ultrastructure of Atypical Fibroxanthoma.** (Eng) Barr, R. J. (Section Dermal Pathology, Univ. California Irvine Medical Center, 101 City Drive S., Orange, CA 92668); Wuerker, R. B.; Graham, J. H. *Cancer* 40(2): 736-743; 1977.

The ultrastructural features of an atypical fibroxanthoma (AFX) are described. The specimen was obtained from a 78-yr-old man in whom an excised AFX recurred twice within a 13-mo period. The tumor appeared to be composed of many xanthomalike giant cells filled with vacuoles. No melanosomes, junctional complexes, or tonofilaments were identified in the sections studied. Many large histiocytes and xanthomalike giant cells showed filopodia or delicate fingerlike cytoplasmic projections on their surfaces, which indicated that the cells were actively pinocytotic. Two types of small cells were identified. The first was similar to ordinary fibroblasts except that the cells appeared morphologically more active. The second type was spindle- to oval-shaped and contained many filopodias similar to those seen on the surface of larger histiocytes. Within the cytoplasm were dense bodies, thin filaments, vacuoles, and other organelles seen in larger giant cells. This cell was considered to be a transition between fibroblasts and xanthomalike giant cells. These ultrastructural features fit those of a fibrohistiocytic reaction. It is recommended that electron microscopy be performed on lesions diagnosed as atypical fibroxanthoma, because ultrastructure studies give the most valid basis for a correct diagnosis. (19 refs.)

77-5253 **Undifferentiated Carcinoma of the Nasopharynx: A Light and Electron Microscopical Study.** (Eng.) Michaels, L. (Dept. Pathology, Inst. Laryngology and Otology, London, England); Hyams, V. J. *Clin Otolaryngol* 2(2): 105-114; 1977.

Light and electron microscopic examination of biopsy material from 29 cases of undifferentiated carcinoma of the nasopharynx showed characteristic features indicating a tumor origin from the overlying squamous epithelium. The tumor cells had a distinctive cellular appearance of "empty" chromatin deficient nuclei, prominent nucleoli and indefinite cytoplasmic margins. Desmosomes and poorly defined tonofilaments were also found. (8 refs.)

77-5254 **An Italian Case of Nasopharyngeal Carcinoma Correlated with Epstein-Barr Virus Specific Antigens.** (Eng) Scolozzi, R. (Istituto di Patologia Speciale Medica e Metodologia Clinica, Universita, Ferrara, Italy); Masucci, G.; Cassai, E.; Pansini, R. *Tumori* 63(4): 381-386; 1977.

A case is reported of a 12-yr-old Italian girl with a metastatic nasopharyngeal carcinoma who had high serum levels of antibody against Epstein-Barr virus (EBV) capsid and nuclear antigens. Antibody titers correlated with the clinical stage of the tumor. A comparison is presented of serum antibody titers to EBV antigens in this case, in cases of infectious mononucleosis and African nasopharyngeal carcinoma, and in healthy controls. (11 refs.)

77-5255 **Biogenic Amines in Nasal Mucosa and Nasal Polyps.** (Eng) Bumsted, R. M. (Dept. Otolaryngology and Maxillofacial Surgery, Univ. Iowa Hosps. and Clinics, Iowa City, IA); El-Ackad, T.; Smith, J. M.; Brody, M. J. *Trans Am Acad Ophthamol Otolaryngol* 84(4): ORL-729-743; 1977.

Biogenic amines (histamine, norepinephrine, and serotonin) were assayed in normal nasal mucosa from 5 patients and in nasal polyps from 23 patients, some with inhalant allergies, asthma, or aspirin sensitivity. Histamine was found only in the mast cells and primarily in the apex of the polyp tissue. Norepinephrine was found around blood vessel walls in the base of the polyps and rarely in the apical region. Serotonin was found in some mast cells throughout the nasal polyp without a differential distribution. In normal mucosa, histamine and serotonin were contained in the mast cells, but norepinephrine was found in association with the blood vessels. There was a significantly higher content of histamine in polyp tissue than in normal mucosa. There was no significant difference in the levels of norepinephrine and serotonin in polyps and normal mucosa. There was no difference in amine levels in polyps from patients without inhalant allergies or asthma, patients with inhalant allergies alone, or patients with inhalant allergies and asthma. In comparison, patients with aspirin sensitivity had the lowest polyp histamine levels. Excessive sympathetic innervation in combination with another stimulus could promote the release of histamine, slow-reacting substance of anaphylaxis (SRS-A), and other kinins and lead to increased vascular permeability, edema, and the leakage of macromolecules out of the vascular system. If the inciting stimulus or mediator imbalance persists, the patient eventually develops nasal polyps; this would explain the greater concentration of histamine in nasal polyps than in normal mucosa. (38 refs.)

77-5256 **Adenomatoid Odontogenic Tumor Resembling a Globulomaxillary Cyst: Light and Electron Microscopic Studies.** (Eng.) Khan, M. Y. (Dept. Pathology, Coll. Medicine and Dentistry New Jersey, New Jersey Medical Sch., 100 Bergen St., Newark, NJ 07103); Kwee, H.; Schneider, L. C.; Saber, I. *J Oral Surg* 35(9): 739-742; 1977.

The case of a 15-yr-old girl with an adenomatoid odontogenic tumor is reported. Various hypotheses on the origin of this rare tumor are presented, including the possibility that it arose as a noncystic tumor from oral epithelium trapped in the line of closure between the medial nasal and maxillary processes. (14 refs.)

77-5257 **Osteogenic Sarcoma of the Maxilla.** (Eng) LiVolsi, V. A. (Dept. Pathology, Yale Univ. Sch. Medicine, 310 Cedar St., New Haven, CT 06510). *Arch Otolaryngol* 103(8): 485-488; 1977.

Six cases of osteogenic sarcoma of the maxilla are reported. Predisposing conditions for three of the patients were trauma, radiation therapy, and a history of Paget's disease; the other three patients had no notable preexisting conditions. Presenting symptoms were a mass in the cheek (3/6), loose teeth on denture (3/6), epistaxis (2/6), and/or diplopia (1/6). Clinicopathologic features of this lesion included: (1) radiologic evidence of an invasive mass with sclerotic or osteogenic processes; (2) gross pathologic evidence of a sclerotic process; and (3) microscopic identification of osteogenic sarcoma, with osteoid formation and calcification, zones of neoplastic cartilage containing many mitotic cells and cells with markedly hyperchromatic nuclei, invasion of the antral mucosa, and destruction of normal preexisting bone. All five of the victims availabe for follow-up died within 5 mo to 3 yr. Autopsy revealed metastatic deposits in the lungs and several bones of 4/5 patients, and massive invasion of the cerebral hemisphere epsilateral to the tumor in the fifth. (18 refs.)

77-5258 **The Spleen in Osteogenic Sarcoma: A Scan and Autopsy Survey.** (Eng) Spencer, R. P. (Dept. Nuclear Medicine, Univ. Connecticut Health Center, Farmington, CT 06032); Flannery, J. T. *Clin Nucl Med* 2(9): 315-317; 1977.

Splenic involvement in osteogenic sarcoma was investigated based on findings from 34 cases (16 males, 18 females, aged 10 to 70 yr) in which a scan and/or autopsy had been performed. The sarcoma originated in the leg (12); ilium (6); tibia (3); vertebra, fibula, maxilla, rib or humerus (2 each) or nasopharynx, foot or skull (1 each). In 25 cases, there was no metastatic involvement; the liver was involved in 2, the spleen and liver in 5 and the spleen only in 2. There was no association between splenic or hepatic metastasis and spleen wt or hepatomegaly. Possible contributing factors to the sarcoma were Paget's disease in four patients, prior mastectomy and irradiation in one, prior irradiation for retinoblastoma in two, and occupational exposure to radium in another. In six patients who had undergone liver-spleen scans, spleen size was normal in five; there was a shift of radiocolloid to the spleen in one patient whose liver was also abnormal. (6 refs.)

77-5259 **Observations of the Pathologist on Precancerous Lesions of the Larynx Integrated with Histological Data and Quantitative Analysis of Nuclear DNA Content.** (Eng) Giarelli, L. (Inst. Pathology, Univ. Trieste, Trieste, Italy); Silvestri, F.; Antonutto, G.; Stanta, G. *Acta Otolaryngol Suppl* 344: 7-18; 1977.

The histology of the normal larynx, identification of precancerous lesions such as leukoplakia, dysplasia, and carcinoma in situ, and the evolution of these lesions toward infiltrative carcinoma are discussed. Quantitative analysis of the nuclear DNA revealed that normal epithelium is predominantly comprised of diploid and (2n) paradiploid cells in the G-1 phase (interphase) of the cell cycle, but that there is a progressive rise toward polyploidy and a prolonged G-2 phase with the evolution of precancerous lesions. Analysis of biopsies marked by severe dysplasia revealed increased numbers of cells with DNA contents ranging from 4n to 6n. A biopsy of a carcinoma in situ had cells with a greater than octaploid (8n) DNA content and an increased percentage of tetraploid cells. These results demonstrate the subversion of a normal cell cycle (increased synthesis and persistence of tetraploid cells by prolongation of the G-2 phase of the cell cycle) and a tendency toward atypical cell proliferation (elements > 4n) due to the abnormal content of nuclear DNA. The lesions that result are believed to represent precancerous and early cancerous stages. (12 refs.)

77-5260 **Tumours in a Cicatricially Altered and Artificial Esophagus.** (Rus.) Kharitonov, L. G. (2nd Dept. Surgery, Central Postgraduate Medical Inst., Moscow, USSR) *Grudn Khir* (1): 76-81; 1977.

Cancer occurred in four cicatricially altered esophaguses 8-34 yr after chemical burns due to sodium hydroxide or sulfuric acid. These cases of squamous keratinized cancer comprised 2% of the patients with esophageal burns and 1.4% of the patients with esophageal cancer. The diagnostic difficulties in interpreting esophagoscopic data are discussed. Recurrent dysphagia, arising many years after burns, is considered the most diagnostically valuable symptom. The esophagus was removed in one patient, and gastrostomy was performed in two. The case report of a patient with a tumor that arose 35-36 yr after total skin esophagoplasty is presented. At autopsy, the tumor was found to be a papilloma. The development of a fistula long after reconstructive surgery may be the first clinical symptom of this type of tumor. (27 refs.)

77-5261 **Surface Morphology and Nucleoside Phosphatase Activity of Rat Liver Epithelial Cells During Oncogenic Transformation In Vitro.** (Eng) Karasaki, S. (Institut du Cancer de Montreal, Centre Hospitalier Notre-Dame, Montreal, Canada H2L 4M1); Simard, A.; de Lamirande, G. *Cancer Res* 37(10): 3516-3525; 1977.

Morphological and biochemical studies of surface membrane alterations associated with in vitro oncogenic transformation were performed with subcultures of seven liver epithelial cell lines from normal and carcinogen-treated Wistar rats. During the preoncogenic phase of passages in vitro, the cells exhibited a gradual increase of surface-located nucleoside triphosphatase activity. When the enzyme activity reached a high level, the cell lines induced tumors upon implantation into newborn Wistar rats. Further biochemical analysis of oncogenic cultures indicated that the ectoenzyme was Mg^{2+}- and Ca^{2+}-dependent nucleoside triphosphatase, similar to the enzyme found in association with contractile proteins. This enzyme was distributed on the entire external membranes of epithelial cells. Scanning electron microscopy of these cells showed reduction of cytoplasmic spreading and microvilli, filopodia, blebs, and ruffles on the surface membranes. Epithelial cells of the preoncogenic cultures were devoid of ectoenzyme activity and had smooth surfaces. Combined cytochemistry and scanning electron microscopy showed a correlation between the phosphatase reaction and the number of microvilli. Transmission electron microscopy of surface carbon replicas allowed visualization of the distribution of enzyme reaction products on ruffles and microvilli. It is proposed that nucleoside phosphatase activity provides an indirect measure of the dynamic surface morphology of oncogenic liver epithelial cells. (34 refs.)

77-5262 **Focal Nodular Hyperplasia of the Liver: Report of Six Patients. Concepts of Surgical Management.** (Eng.) Catalano, P. W. (Dept. Surgery, Ohio State Univ. Coll. Medicine, Columbus, OH); Early, M. E.; Topolosky, H. W.; Martin, E. W.; Carey, L. C. *Cancer* 39(2): 587-591; 1977.

Six case reports are presented of women, ages 21 to 44 yr, with focal nodular hyperplasia of the liver. All had taken oral contraceptives for an av of 5 yr, although no correlation of the disease with any specific ingested hormone could be established. (9 refs.)

77-5263 **Hepatocellular Carcinoma in a Woman on Long-Term Oral Contraceptives.** (Eng) Pryor, A. C. (Dept. Medicine, Mount Zion Hosp. and Medical Center, P. O. Box 7921, San Francisco, CA 94120); Cohen, R. J.; Goldman, R. L. *Cancer* 40(2): 884-888; 1977.

A case of fatal hepatocellular carcinoma developed in a 32-yr-old woman who had taken oral contraceptives continuously for 12 yr. Nine months before hospitalization, the patient began having sporadic episodes of epigastric and right upper quadrant pain that grew more severe. At the time of admission, the clinical impression was acute and chronic cholecystitis and cholelithiasis. Exploratory laparotomy disclosed a large tumor mass involving both lobes of the liver. Intensive chemotherapy failed to arrest tumor growth, and the patient died 15 mo after diagnosis of hepatic failure. The histologic features were those of a well-differentiated hepatocellular carcinoma. The relationship between the development of hepatocellular carcinoma and the use of oral contraceptives is speculative, but there is evidence in the literature to indicate that oral contraceptives have the ability to cause profound morphological and functional changes in the hepatic cell. Other cases of malignant hepatic neoplasms associated with oral contraceptive therapy are now being reported, some appearing to have arisen in benign tumors. Although the instances of hepatocellular malignancies associated with oral contraceptive therapy are limited, the association may be more than random in view of the fact that hepatocellular carcinoma usually appears in older adults or in association with liver damage, contrasting with recently published cases and with the patient described in this report. (16 refs.)

77-5264 **Persistence of Endocrine Cells Associated with Immunoinduced Exocrine Pancreatic Carcinomas: Insulin, Glucagon, and Somatostatin Cells.** (Fre.) Andre-Thomas, J. (Centre de Physiologie cellulaire, Universite Pierre-et-Marie-Curie, 7, quai Saint-Bernard, 75005 Paris, France); Dubois, M. P.; Hollande, E. *CR Acad Sci [D] (Paris)* 284(23): 2385-2390; 1977.

Direct and indirect immunochemical techniques demonstrated normal insulin (B), glucagon (A), and somatostatin (D) endocrine cells in immunoinduced exocrine pancreatic carcinomas of mice. Immunocytochemical studies revealed B cells in the islets of Langerhans and, also, in the anaplastic carcinomatous tissue. These cells mostly had a large granular cytoplasm. Large numbers of A cells were also found in the islets of Langerhans, mainly at the periphery. A small number of these cells were detected in the malignant exocrine structures and lymphoblastic nodules. D cells, isolated or in small groups, were found in the acinous residue and, to a lesser extent, in the exocrine tissue. However, these cells were not found in anaplastic carcinomatous tissue or in the proliferating and infiltrating canalicular sheet. Infrastructural studies during the early stages of malignancy showed no degenerative changes in the endocrine cells, except for the appearance of granules. In the second stage, all three types of cells were seen in the islets of Langerhans; they contained numerous granules and the Golgi apparatus was quite dilated. In the late stages the A cells were rich in granules and they had an irregular membrane. In conclusion, the three types of endocrine cells persist and are not destroyed by cancer. (23 refs.)

77-5265 **Biliary Carcinoma Associated with Biliary Cysts.** (Eng) Flanigan, D. P. (Dept. General Surgery, St. Joseph Mercy Hosp., P. O. Box 995. Ann Arbor, MI 48106). *Cancer* 40(2): 880-883; 1977.

The 24th reported case of biliary carcinoma associated with biliary cystic disease is given, and the previously reported cases are reviewed and analyzed. A 26-yr-old man presented with right upper quadrant pain following a fatty meal. No abnormalities other than cholecystitis were found and he did well for 3 yr, at which time the symptoms recurred. At operation, a biliary cyst involving the common bile duct and distal common hepatic duct was found. The cyst contained stones, but no neoplasm was observed. Several episodes of obstructive jaundice occurred 5 yr later. At a second operation, a well-differentiated adenocarcinoma was found. Resection was not feasible, and the patient died 2 mo later. Analysis of the other cases in which carcinoma developed showed that in 25%, stones were present in the cyst. The most common cell type was adenocarcinoma (70%), and the most common tumor site was the posterior cyst wall (57%). Half of the patients developed carcinoma an av of 4 yr following an internal drainage procedure for biliary cystic disease. Of the reported cases of biliary cysts associated with the cystlithiasis (19), one-third had associated biliary carcinoma. In only two patients was the tumor within the limits of curative resection at the time of diagnosis. It is suggested that excisional therapy be performed when possible in all patients with biliary cystic disease, especially those with associated cystlithiasis. (26 refs.)

77-5266 **Use of Endoscopy to Diagnose Precancerous Diseases and Stomach Cancer in Outpatient Clinics.** (Rus.) Pshenichnyi, M. A. (Dept. Surgery Digestive Tract, Rovno Oblast Hosp., Rovno, USSR); Borovyi, E. M.; Kiriachkova, A. I.; Sivyi, N. Iu. *Vrach Delo*(11): 85-87; 1976.

The efficacy of endoscopy was evaluated in 123 outpatients with various stomach lesions. X-ray diagnosis was chronic gastritis (53), gastric ulcer (38), stomach cancer (22), possible stomach cancer (10). At endoscopy, the diagnosis of chronic gastritis was confirmed in 33/53 patients (5 had gastric ulcer, 7 stomach cancer, 5 no pathologic changes, and 2 could not undergo endoscopy). The diagnosis of gastric ulcer was confirmed in 16/38 patients (10 had chronic gastritis, 7 stomach cancer, 3 no pathology); stomach cancer was confirmed in 12/22 patients (3 had gastric ulcer, 1 gastric polyposis, 4 chronic gastritis, 1 no pathology) and in 3/10 patients (2 had gastric ulcer, 4 chronic gastritis, 1 no pathology) with a tentative diagnosis of stomach cancer. (no refs.)

77-5267 **Nonspecific Hormonal Reaction in Patients with Gastric Cancer.** (Rus.) Vereschchagina, G. V. (Moscow Scientific Res. Inst. Roentgenology and Radiology, Ministry Public Health Russian SSR, Moscow, USSR) Zubovskii, G. A.; Goloskov, N. P.; Sutiagin, A. G. *Sov Med* (2): 78-82; 1977.

Gastric cancer Stages I-IV were diagnosed by roentgenoendoscopic studies and confirmed by gastrobiopsy or surgery in 37 patients (39-73 yr old). Serum levels of cortisol, insulin, somatotropic hormone (STH), thyrotropic hormone (TTH), total thyroxine, and triiodothyronine (TIT) were determined along with the coefficient of relative thyroxine effectiveness (CTE) and the TIT binding capacity of the serum. Control groups had benign gastric tumors (polyps, leiomyomas), ulcers, or chronic gastritis. The thyroxine:TIT and TTH:TIT ratios were affected to some extent in the early stages of gastric cancer. Insulin levels decreased progressively with cancer development to 11.8 microunits (μU) from control levels of 23.2 μU/ml. STH and TTH levels increased to 1.45 and 3.13 nanograms (ng)/ml, respectively, from control levels of 0.3 and 2.23 ng/ml, respectively. Thyroxine levels and CTE increased, but TIT levels decreased. Serum cortisol levels were similar to those of controls. It is proposed that the disturbances in hormonal homeostasis noted in the early stages promote the development of gastric cancer. The increases or decreases in hormone levels in the later stages may be a host response to cancer development. (19 refs.)

77-5268 **Gardner's Syndrome and Duodenal Adenocarcinoma. Study of a Case and Literature Review.** (Fre) Suzanne, J. (Laboratoire d'Anatomie Pathologique, Centre Hospitalier et Universitaire, place Saint-Jacques, F 25030 Besancon Cedex, France); Camelot, G.; Miguet, J. P.; Carbillet, J. P.; Gillet, M.; Carayon, P.; Gisselbrecht, H. *Gastroenterol Clin Biol* 1(5): 455-460; 1977.

Gardner's syndrome and duodenal adenocarcinoma associated with duodenal polyps occurred in a 47-yr-old man. Previously, the patient had a total colectomy for multiple endocrine adenomatosis without malignant changes. He presented with marked hepatomegaly and was hospitalized because of cholestatic icterus and emaciation. Hypotonic duodenography revealed a rounded and regular gap facing the ampulla of Vater, and duodenoscopy showed a duodenal mucosa that was very congested, with multiple polypoid formations and a large, white, smooth-surfaced tumor. A diagnosis of benign adenoma was made by biopsy. Laparotomy showed a green liver without visible metastases and an ampullary tumor. Multiple polypoid granulations covered the entire duodenum plus the first jejunal loop, and numerous white tumors were seen in the mesentery. A cephalic duodenopancreatectomy with biliary derivation was performed, and postoperative histological examination confirmed an ampullary duodenal adenocarcinoma. The intramesenteric tumors were comprised of well-differentiated fat cells and of fibrous tissue devoid of cells but rich in collagenous fiber. Postoperatively, an occlusive condition occurred 3 mo later that required a laparotomy. Mesenteric fibrosis with numerous adhesions plus edematous and inflammatory streaks in the pancreatojejunal region were seen. The patient died 6 mo later. At least 2/5 children of the subject had genetic anomalies. According to literature cases, Gardner's syndrome is usually associated with osteoma, which this patient did not have. (16 refs.)

77-5269 **Periampullary Malignancy in Gardner's Syndrome.** (Eng) Jones, T. R. (Dept. Surgery, Louisiana State Univ. Medical Center, 1542 Tulane Ave., New Orleans, LA 70112); Nance, F. C. *Ann Surg* 185(5): 565-573; 1977.

The cases of three women, aged 67, 49, and 63, each with a familial polyposis coli and associated periampullary malignancy are presented. It is believed that the periampullary carcinoma is an extracolonic manifestation of Gardner's syndrome and should be considered a variant of the disease. The literature is reviewed. (53 refs.)

77-5270 **Association of *Streptococcus bovis* with Carcinoma of the Colon.** (Eng) Klein, R. S. (Dept. Medicine, Div. Infectious Diseases, Montefiore Hosp. and Medical Center, 111 E. 210th St., Bronx, NY 10467); Recco, R. A.; Catalano, M. T.; Edberg, S. C.; Casey, J. I.; Steigbigel, N. H. *N Engl J Med* 297(15): 800-802; 1977.

A search was made for the presence of group D nonenterococcal (DNE) streptococci in patients with various malignant diseases, particularly of the gastrointestinal tract, and controls. DNE were found in 11/105 controls, 35/63 patients with colonic carcinoma, 7/25 patients with inflammatory bowel disease, 5/37 patients with other gastrointestinal disease, 3/12 patients with a history of colonic carcinoma, 1/15 patients with a recent barium enema study and 4/21 patients with non-colonic neoplasms (breast, esophageal, seminoma, cholangiocarcinoma). Lactose fermentation indicated that all DNE were *Streptococcus bovis*. The carrier state was unrelated to age, hospitalization status, colonic stasis, gastrointestinal bleeding or barium enema examination. The prevalence of *S. bovis* in colonic carcinoma reached 56%, a significant increase as compared to controls and to other patients. The implications of these findings, particularly in regard to DNE endocarditis, are discussed. (18 refs.)

77-5271 **Basosquamous (Transitional Cloacogenic) Carcinoma of the Sigmoid Colon.** (Eng) Strate, R. W. (Dept. Pathology, Univ. Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284); Richardson, J. D.; Bannayan, G. A. *Cancer* 40(3): 1234-1239; 1977.

The case is reported of a 59-yr-old woman with a basosquamous transitional cloacogenic carcinoma in the sigmoid colon above the pelvic brim at the peritoneal reflection. Palliative surgery was performed; liver metastases were noted. It is suggested that a totipotent "basal" cell could be responsible for tumor occurrence at this site. The tumor also produced parathyroid hormone and possible ACTH. (19 refs.)

77-5272 **Neoplasms of the Large Bowel Following Ureterosigmoidostomy.** (Eng.) Sooriyaarachchi, G. S. (Dept. Internal Medicine, Rockford Clinic, 2300 N. Rockton Ave., Rockford, IL 61101); Johnson, R. O.; Carbone, P. P. *Arch Surg* 112(10): 1174-1177; 1977.

The case of a 43-yr-old man who developed poorly differentiated adenocarcinoma of the rectum 37 yr after ureterosigmoidostomy is presented. Several hypotheses for the development of neoplasms at the site of anastomosis are presented. The literature on similar cases is reviewed. (42 refs.)

77-5273 **Neoplasms at the Site of Ureterocolic Anastomosis.** (Eng.) Mogg, R. A. (215 Newport Road, Cardiff, CF2 1AJ, Wales). *Br J Surg* 64(10): 758-761; 1977.

The case reports are presented of three patients, aged 35, 26, and 43 yr, who developed tumors at the site of previous ureterocolic anastomoses. The tumors appeared 15 to 34 yr after the original anastomosis. The etiology of the cancer in these patients is unknown. (26 refs.)

77-5274 **Production of Reversible Papillary Proliferation of the Urinary Bladder in Rats.** (Eng.) Shirai, T. (First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho Mizuho-ku, Nagoya 467, Japan); Cohen, S. M.; Fukushima, S.; Ito, N. *Gann* 68(4): 521-522; 1977.

Reversible papillary proliferation was induced in the urinary bladder epithelium of male Wistar rats by applying a steel rod, frozen to -78 C, for a few seconds. This method allows study of regenerative hyperplasia without the administration of cytotoxic chemicals; it can also be used in organs such as the stomach and colon. Multiple exposures can be repeated as needed. (3 refs.)

77-5275 **Histopathological Evaluation of the Inhibition of Rat Bladder Carcinogenesis by 13-*cis*-Retinoic Acid.** (Eng.) Squire, R. A. (NCI, Bethesda, MD 20014); Sporn, M. B.; Brown, C. C.; Smith, J. M.; Wenk, M. L.; Springer, S. *Cancer Res* 37(8, part 2): 2930-2936; 1977.

The inhibition of N-methyl-N-nitrosourea (NMU)-induced bladder cancers in female Wistar/Lewis rats by 13-*cis*-retinoic acid was investigated. The tumors were induced by three doses of NMU instilled directly into the bladder. The rats were then fed with either 120 or 300 mg/kg of the acid in the diet. Of 23 rats in the control group, 13 developed bladder neoplasms; of the 10 bladder carcinomas, 7 were transitional cell and 4 were squamous. Of the 44 animals that received the acid in the diet at 120 mg/kg, 19 developed neoplasms; of the 15 bladder carcinomas, 13 were transitional cell and 5 were squamous. Of the 43 rats receiving 300 mg/kg, 16 developed neoplasms; of the 12 bladder carcinomas, there were 10 transitional cell and 3 squamous carcinomas. The inhibitory effect of 13-*cis*-retinoic acid on the development of squamous dedifferentiation was considered especially significant. (7 refs.)

77-5276 **Malignant Transformation of Urinary Bladder in Humans and in N-[4-(5-Nitro-2-furyl)-2-thiazolyl]formamide-exposed Fischer Rats: Ultrastructure of the Major Components of the Permeability Barrier.** (Eng.) Merk, F. B. (Dept. Pathology, Tufts Univ. Sch. Medicine, Boston, MA 02111); Pauli, B. U.; Jacobs, J. B.; Alroy, J.; Friedell, G. H.; Weinstein, R. S. *Cancer Res* 37(8/part 2): 2843-2853; 1977.

The ultrastructure of the permeability barrier in the urinary bladder was investigated in human transitional cell carcinomas and in comparable N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide (FANFT)-induced tumors in male Fischer rats. FANFT was administered ad libitum as 0.2% of powdered chow for 25 wk. Human tumors were obtained from specimens, biopsy and autopsy with cystoscopic samples as controls. Tight junctions (zonulae occludentes) of normal rat cells were observed to have three to five intramembrane fibrils; however, in FANFT-induced tumors after 25 wk on the diet, the tight junctions were attenuated to a single fibril. Invasive carcinomas frequently had incomplete, discontinuous junctions. In normal humans, tight junctions were complete and well developed. In low-grade noninvasive human transitional cell tumors, the junctions were complete but attenuated. These junctions were discontinuous in high-grade invasive tumors, appearing as maculae occludentes. Because the number and distribution of intramembrane fibrils is correlated with the transepithelial permeability, it is suggested that incomplete formation and/or rapid turnover of the junctions results in increased permeability in transitional cell carcinoma. (35 refs.)

77-5277 **Freeze-fracture Observations on the Membranes and Junctions in Human Prostatic Carcinoma and Benign Prostatic Hypertrophy.** (Eng) Sinha, A. A. (Building 49, Room 207, Veterans Admin. Hosp., Minneapolis, MN 55417); Bentley, M. D.; Blackard, C. E. *Cancer* 40(3): 1182-1188; 1977.

The plasma membranes and junctional complexes of human benign prostatic hypertrophy (BPH) and prostatic adenocarcinoma were studied based on freeze-fracture studies of biopsy-obtained specimens. Columnar cells of prostatic cancer had a loose meshwork of ridges and grooves and many isolated, short, disorganized strands of tight junctions suggesting that the latter were defective. In BPH, the ridges and grooves were numerous and compact. Cancerous cells had more irregularly shaped and distributed desmosomes than cells from patients with BPH. It is suggested that defective desmosomes facilitated migration of acinar cells into the stroma. A brief comparison of these findings with those from tissue culture studies is presented. (24 refs.)

77-5278 **Primary Papillary Carcinoma of the Prostate: Report of a Histopathologic, Cytologic and Electron Microscopic Study on One Case.** (Eng.) Epstein, N. A. (South African Inst. Medical Res., P.O. Box 1038, Johannesburg 2000, South Africa). *Acta Cytol (Baltimore)* 21(4): 543-546; 1977.

The case of a 65-yr-old man with primary papillary carcinoma of the prostate is presented. Detailed study suggested that this tumor arose within the prostate from cells that did not secrete acid phosphatase. This carcinoma fits into the same classification category as adenocarcinoma of the prostate, due to similar mode of infiltration of the stroma. (12 refs.)

77-5279 **Ultrastructure of Gonadoblastoma and Disgerminoma (Seminoma) in a Patient with XY Gonadal Dysgenesis.** (Eng) Bjersing, L. (Dept. Pathology, Univ. Umea, S-901 87 Umea, Sweden); Cajander, S. *Cancer* 40(3): 1127-1137; 1977.

The results of light and electron microscopic studies of tissue from a 19-yr-old phenotypic female with incomplete XY gonadal dysgenesis, gonadoblastoma and disgerminoma are presented. The most characteristic features of the gonadoblastoma were the rounded nests, composed of large germ cell-like elements mixed with Sertoli-like cells. The hyaline material around the latter consisted of closely packed, concentric membranes, similar to the basal laminae of seminiferous tubules. In addition, gonadoblastomal elements were observed in enlarged tumoral structures in transitional zones, suggesting that gonadoblastomas originate inside tubules of dysgenetic cells. The concentric membrane structures may reflect increased hyperplasia and cell death of Sertoli cells. (46 refs.)

77-5280 **Breast Cancer in a Father and Son.** (Eng.) Manheimer, L. H. (No affiliation given). *Breast* 3(2): 21-23; 1977.

An unusual case is presented of adenocarcinoma in the left breast of a 49-yr-old man whose father had had carcinoma in both breasts. A family cancer pedigree, chromosome analysis, and results of hormonal assays are presented. (5 refs.)

77-5281 **Comparative Chromosome Study of Normal Mammary Tissue, Carcinogen-induced Mammary Tumors, and Hyperplastic Alveolar Nodules in the Rat: Brief Communication.** (Eng.) Takahashi, Y. (Dept. Breast Surgery, Roswell Park Memorial Inst., Buffalo, NY 14263); Sinha, D. K.; Dao, T. L. *J Natl Cancer Inst* 59(3): 1007-1012; 1977.

Chromosomal constituents of 101 normal mammary gland cells, 122 hyperplastic alveolar nodule (HAN) cells, and 360 cells from 11 different 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary tumors in 64 to 73-day-old female WF rats were examined. Both normal mammary and HAN cells showed the usual diploid karyotype patterns. Abnormalities such as aneuploidy, pseudodiploidy, and polyploidy and structural aberrations such as breaks and translocations occurred frequently (30%) in the DMBA-induced tumor cells. These results suggest that the chromosome constituents of HAN cells are similar to those of normal mammary epithelial cells. (12 refs.)

77-5282 **Carcinoma In Situ of the Breast.** (Eng) Carter, D. (Dept. Pathology, Brady Memorial Lab., Yale Univ., 310 Cedar St., New Haven, CT 06510); Smith, R. R. *Cancer* 40(3): 1189-1193; 1977.

In a series of 87 patients with in situ breast carcinoma, 38 had intraductal carcinoma and 49 had lobular carcinoma. Of the former, all underwent mastectomy; residual intraductal carcinoma was found in 25 and invasive duct carcinoma was found in 7. Four patients underwent bilateral mastectomy, and in situ lobular carcinoma was found in addition to intraductal disease in three cases and residually in the fourth. Four patients had lymph node metastases. All 49 patients with in situ lobular carcinoma also underwent mastectomy; residual disease was found in 31 and invasive in 3. Five patients underwent bilateral mastectomy; all had residual in situ carcinoma in at least one breast; three had bilateral in situ carcinoma; none had invasion. One patient had lymph node metastases. Three patients in the intraductal group died of cancer as compared to none in the lobular group. In conclusion, in situ carcinoma is regarded as a noninvasive process with the intraductal form synchronously associated with invasive cancer; when in situ lobular carcinoma appears in both breasts, there is a significant risk that invasion may occur. (12 refs.)

77-5283 **Carcinoma Arising in the Wall of a Breast Cyst During Pregnancy.** (Eng) Roth, J. A. (Dept. Surgery, UCLA Sch. Medicine, Los Angeles, CA 90024); Feinberg, M.; McAvoy, J. M. *Ann Surg* 185(2): 247-250; 1977.

A 23-yr-old woman developed a carcinoma in the wall of a breast cyst during her third pregnancy. None of the seven previously reported cases of carcinoma in a breast cyst were reported during pregnancy. The relationship between carcinoma and fibrocystic disease, and the influence of pregnancy and age on the prognosis are considered. (41 refs.)

77-5284 **Androgenetic Origin of Hydatidiform Mole.** (Eng) Kajii, T. (Genetic and Endocrine Unit, Dept. Pediatric, State Univ. New York, Upstate Medical Center, Syracuse, NY 13210); Ohama, K. *Nature* 268(5621): 633-634; 1977.

Cytogenetic analysis of the hydatidiform mole revealed that its karyotype is predominantly, if not exclusively, 46,XX, and that it receives only paternal chromosomes and therefore is androgenetic in origin. Karyotyping of 20 moles, 10 of Caucasian origin and 10 of Japanese origin, showed each of them to be 46,XX. The mode of inheritance of the molar chromosomes of seven males was studied with the use of fluorescence Q- and R-banding polymorphisms as markers. All 7 pairs of chromosomes (Nos. 3,4,13,14,15,21,and 22) from each of the 7 moles (total 49 pairs of homologous chromosomes) were homologous for banding polymorphisms. In 26 pairs of chromosomes, neither of the maternal homologs was transmitted to the mole, but in 20/26 pairs, a paternal chromosome was shown to be inherited in duplicate. These findings demonstrate that the moles are androgenetic in origin. The androgenesis arises from fertilization of an ovum with an inactivated or absent nucleus by a diploid or a hoploid sperm, followed by duplication of its chromosomes. The high malignancy rate in patients with hydatidiform mole may result from the presence of a homozygous recessive mutant gene controlling cell growth that might allow the cells to escape from normal growth control. (7 refs.)

77-5285 **Ovarian Teratomas in Mice Are Derived from Oocytes That Have Completed the First Meiotic Division.** (Eng.) Eppig, J. J. (Jackson Lab., Bar Harbor, ME 04609); Kozak, L. P.; Eicher, E. M.; Stevens, L. C. *Nature* 269(5628): 517-518; 1977.

A study of ovarian teratoma in (LT/Sv x LTXBJ)F_1 mice indicated that the tumors originated in oocytes following the first meiotic division. It is speculated that either these diploids underwent karyokinesis in the second meiotic division without cytokinesis, or that there was a fusion of the second polar body with the ovum. (2 refs.)

77-5286 **Ovarian Extraembryonal Teratoma. I. Endodermal Sinus Tumor.** (Eng.) Jimerson, G. K. (Dept. Gynecology, Post Office Box 26901, Oklahoma City, OK 73190) Woodruff, J. D. *Am J Obstet Gynecol* 127(1): 73-79; 1977.

A series of 41 cases of pure endodermal sinus ovarian tumors that occurred in females ranging in age from 14 mo to 40 yr is described. (12 refs.)

77-5287 **The Residual Adnexa--Asset or Liability?** (Eng.) Funt, M. I. (Dept. Obstetrics and Gynecology, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT 06510); Benigno, B. B.; Thompson, J. D. *Am J Obstet Gynecol* 129(3): 251-254; 1977.

Of 922 patients who underwent abdominal hysterectomy for benign disease with conservation of one or both adnexa, only 13 (1.4%) underwent further exploration for adnexal pathology; 10 of these patients had corpus luteum cysts. No ovarian malignancy occurred in the short period of follow-up. Thus conservation of ovarian function is recommended in premenopausal women. (15 refs.)

77-5288 **Serous Tumors of the Ovary. I. Ultrastructural and Histochemical Studies of the Epithelium of the Benign Serous Neoplasms, Serous Cystadenoma and Serous Cystadenofibroma.** (Eng) Fenoglio, C. M. (630 W. 168th St., New York, NY 10032); Castadot, M. J.; Ferenczy, A.; Cottral, G. A.; Richart, R. M. *Gynecol Oncol* 5(3): 203-218; 1977.

Ultrastructural and histochemical studies were made of 23 benign serous neoplasms, a series that included both cystadenomas and cystadenofibromas, in order to elucidate the histogenesis of cystomas and cystadenocarcinomas. The remarkable similarity of the fine structure of the epithelium lining the serous cystadenomas and cystadenofibromas to that of the fallopian tube supported the proposed histiogenesis of these lesions from metaplasia of the celomic epithelial inclusion cysts. A mucinous component of well-developed endocervical cells was seen in 3/23 neoplasms. This mixture of cell types was consistent with the hypothesis of the multicellular potential of the celomic epithelial inclusion cyst. It suggested (1) that multiple metaplastic cell types may occur with the predominance of one in a given lesion or (2) that there may be multipotential cells present in the generative compartment of the cystomas that may from time to time undergo metaplasia in a direction different from that taken by most cells lining the lesion. Ultrastructural studies indicated that the active accumulation of fluid in the serous neoplasms is apparently accomplished, at least in part, by pinocytosis on both the basal and apical portions of the cells. In some instances, intercellular accumulations of fluid were prominent, and their fine structural appearance resembled that of mesotheliomas. (19 refs.)

77-5289 **Uterine Leiomyoblastoma. Ultrastructural and Cytological Studies.** (Eng) Chang, V. (Inst. Pathology, Case Western Reserve Univ., Cleveland, OH 44106); Aikawa, M.; Druet, R. *Cancer* 39(4): 1563-1569; 1977.

The case is presented of a 44-yr-old woman with a uterine leiomyoblastoma that developed 16 yr after radiation treatment for a non-keratinizing squamous cell carcinoma of the uterine cervix. Cytological and ultrastructural studies indicated that the tumor arose in the smooth muscle layer. (14 refs.)

77-5290 **Cytogenetic Studies of Human Endometrial Carcinomas by Means of Tissue Culture.** (Eng) Kuramoto, H. (Dept. Obstetrics and Gynecology, Sch. Medicine, Kitasato Univ., Sagamihara, Japan); Hamano, M. *Acta Cytol (Baltimore)* 21(4): 559-565; 1977.

Cytogenetic studies were attempted on tissue cultures from 42 primary uterine endometrial carcinomas. Of these, 17 were eventually analyzed. Twelve cases (75%) had a peak number of 46 chromosomes; the distribution ranged from hypo- to hyperdiploid. Karyotypes of 13 patients showed minimal structural alterations, while 4 had an apparent aberrant chromosome larger than A_1. In the first group, although no apparent structural alterations were observed, numerical alterations and variant chromosomes with minimum structural alterations (eg, heteromorphism, minimum alterations of arm ratio, gapping) were seen at random. Only one marker chromosome was identified among the four cases with unclassified and markedly aberrant chromosomes. No tendency between histologic grading and the presence of structural alteration was observed. It is concluded that carcinomas of the corpus uteri consist mainly of cells with a pseudo-diploid number and that a chromosomal alteration not revealed by conventional analytical methods may play a role in the etiology of this disease. (16 refs.)

77-5291 **Surface Ultrastructural Response of the Human Uterine Lining Epithelium to Hormonal Environment. A Scanning Electron Microscopic Study.** (Eng.) Ferenczy, A. (Dept. Pathology, Jewish General Hosp., 3755 Cote St. Catherine Road, Montreal, Quebec, H3T 1E2, Canada). *Acta Cytol (Baltimore)* 21(4): 566-572; 1977.

The surface architecture and hormonal response of uterine epithelial cells were investigated electron microscopically in human endometrial tissue (normal, atrophic, hyperplastic, and neoplastic, and including specimens from women treated with 17β-estradiol). Observations of the cilia and villi suggested that their formation was chiefly influenced by endogenous estrogens. The absence of cilia and villi in adenocarcinoma and other malignancies may result from loss of hormonal receptors. This in turn could be related to a loss of contact inhibition and adhesiveness, and to an increase in mobility. (23 refs.)

77-5292 **On the Pathogenesis of Kuttner Tumors of the Submandibular Gland - Analysis of 349 Cases with Chronic Sialadenitis of the Submandibular Gland.** (Ger.) Seifert, G. (Pathologisches Institut der Universitat, D-2000 Hamburg 20, Martinistrasse 52, W. Germany); Donath, K. *HNO* 25(3): 81-92; 1977.

Pathologic and histologic findings were reviewed in 349 patients (185 males, 164 females, from infancy to over 80 yr of age) with Kuttner tumor (chronic sialadenitis of the submaxillary gland). The most common symptoms were painful swelling of the gland and subfebrility of 3-24 mo duration. Case histories revealed the following common complaints: recurrent respiratory tract infections; gall, urinary, and kidney stones; diabetes mellitus; thyroid disease; renal dysfunction; and defective denture. Nicotine and alcohol abuse were sporadic. In 143 cases, a sialolithiasis of the submandibular gland occurred spontaneously; sialoliths frequently recurred 18 mo after removal. Four stages were identified: focal sialadenitis, diffuse lymphocytic sialadenitis with salivary gland fibrosis, chronic sclerosing sialadenitis with salivary gland sclerosis, and chronic progressive sialadenitis with salivary gland cirrhosis. The first stage was characterized by periductal lymphocytic infiltration, ductal ectasia and alteration of the duct lumens. The second and third stages were characterized by inflammation of the lymph follicles, ductal alteration, parenchymal reduction, and an increase in interstitial connective tissue. In the fourth stage, cirrhotic gland transformation and continuing parenchymal loss were found. Two etiological factors were recognized as important: an initial secretory disturbance with obstructive electrolyte sialadenitis and an immune response culminating in obstructive immunosialadenitis. (35 refs.)

77-5293 **Transplantable Murine Salivary Gland Carcinoma (Myoepithelioma). I. Biologic Behavior and Ultrastructural Features.** (Eng.) Delaney, W. E. (Dept. Medicine, Lankenau Hosp., Philadelphia, PA 19151). *J Natl Cancer Inst* 58(1): 61-65; 1977.

Three salivary gland adenocarcinomas arose spontaneously in female BALB/c mice being maintained for plasmacytoma (MOPC) investigations. Only one of the hosts was MOPC-bearing. The initial carcinomas clearly originated from the salivary gland, not the breast, and did not resemble plasma cell lesions. The submandibular gland was the site of origin in each case. The lesions were identical to those described previously in strains A and C mice as myoepitheliomas, with intracellular fibrils positive by phosphotungstic acid-hematoxylin (PTAH) stain. The three salivary gland carcinomas were serially transplanted for 28, 29, and 14 generations, respectively. The tumor take was almost 100%, and the hosts died within 6-12 wk, with metastasis to the peritoneum and liver. A myeloproliferative reaction characterized by changes occurred regularly during tumor growth. Each transplant generation was identical to its original primary by light and electron microscopy. In their growth pattern, the tumors resembled sarcomas with large areas of spindle cells. Ultrastructurally, the neoplastic cells contained the organelles of acinar and possibly ductal cells and exhibited varying degrees of synthetic and secretory activity. Numerous desmosomes were seen in all cells; coarse filaments and fine fibrils were common in cells exhibiting lesser degrees of secretion. The filaments most likely represented the PTAH-positive intracellular fibrils observed by light microscopy. All tumors had numerous cells with resting features. (23 refs.)

77-5294 **Microfollicular Thyroid Carcinoma with Amyloid Rich Stroma, Resembling the Medullary Carcinoma of the Thyroid (MCT).** (Eng) Valenta, L. J. (Dept. Medicine, Univ. California Irvine Medical Center, Orange, CA 92668); Michel-Bechet, M.; Mattson, J. C.; Singer, F. R. *Cancer* 39(4): 1573-1586; 1977.

The case of a 55-yr-old man with a slow-growing thyroid tumor is presented. The tumor was a solid carcinoma with partial microfollicular differentiation; light-microscopically, however, it resembled medullary carcinoma of the thyroid with amyloid rich stroma. There was insufficient evidence to suggest a C cell origin. (61 refs.)

77-5295 **Prevalence of Endocrine Neoplasia Syndromes in Genetic Studies of Parathyroid Tumors.** (Eng) Jackson, C. E. (Dept. Medicine, Henry Ford Hosp., Detroit, MI 48202); Frame, B.; Block, M. A. *Prog Cancer Res Ther* 3: 205-208; 1977.

A study of the families of 91/100 consecutive patients with parathyroid tumors revealed that 10 of them had other family members who were affected. Pedigrees are presented of three families with evidence of multiple endocrine neoplasia type I (MEN I) and two families with MEN II. In addition, familial hyperparathyroidism alone was found in five kindreds. Two patients with parathyroid carcinoma were encountered in this series; the limited studies possible in their families revealed no other cases of hyperparathyroidism. Combinations of hyperplasia, adenoma, and carcinoma of the parathyroid glands may occur in a single individual and in different members of the same family. (9 refs.)

77-5296 **Primary Reticulum Cell Sarcoma of the Brain in Wiskott-Aldrich Syndrome. Report of a Case.** (Eng.) Model, L. M. (1125 Grant Blvd., Apt D, Syracuse, NY 13203). *Arch Neurol* 34(10): 633-635; 1977.

The case of a 3.5-yr-old boy with Wiskott-Aldrich syndrome who developed a reticulum cell sarcoma of the brain is presented. Since patients with this syndrome have a 10% chance of developing cancer, it is postulated that their immune deficiencies are related to tumor development. (6 refs.)

77-5297 **Malignant Granular Cell Tumor of the Radial Nerve. An Autopsy Observation with Electron Microscopic and Tissue Culture Studies.** (Eng) Usui, M. (Dept. Orthopedic Surgery, Hokkaido Univ., Sch. Medicine, Kita-14-jo, Nishi-5-chome, Kita-ku, Sapporo, Japan); Ishii, S.; Yamawaki, S.; Sasaki, T.; Minami, A.; Hizawa, K. *Cancer* 39(4): 1547-1555; 1977.

The case of a 34-yr-old man with a granular cell tumor of the left upper arm is presented. In spite of surgery, the tumor metastasized to the lungs and lymph nodes. Electron microscopic and tissue culture studies, and a review of the literature suggest that this tumor arose in the radial nerve. (20 refs.)

77-5298 **Bronchopulmonary Cancers and Emphysem Bullae.** (Fre.) Galy, P. (Hopital cardiovasculaire et pneumologique, rue du Doyen-Lepine, 69000 Lyon-Bron, France); Brune, J.; Kassoulides, I. *Rev Fr Mal Respir* 5(4): 441-442; 1977.

Brief observations on the occurrence of bronchopulmonary cancer in seven men aged 25-57 yr with existent emphysema bullae, mostly the bi-apical type, are given. The clinical symptoms were not unique: hemoptysis, coughing, pain, and emaciation. The cancer was discovered in one patient upon systematic examination. The main radiological symptom was a somewhat irregular opacity with spicules. At times an irregular and extensive mass was seen in contact with the bullae. Histologically, epidermoid, glandular, and cubic or nondifferentiated epitheliomas were present in five patients, whereas one had a histiocytosarcoma and one had a mucoid adenocarcinoma. It is concluded that the occurrence of bronchopulmonary cancer with emphysema bullae is too great to be attributed to chance. (2 refs.)

77-5299 **Amylase-producing Lung Cancer. Ultrastructural and Biochemical Studies.** (Eng) Yokoyama, M. (Dept. Internal Medicine, Section 3, Sapporo Medical Coll., Sapporo, Japan); Natsuizaka, T.; Ishii, Y.; Ohshima, S.; Kasagi, A.; Tateno, S. *Cancer* 40(2): 766-772; 1977.

A lung cancer with elevated amylase activity in serum, urine, and tumor tissue was studied electron microscopically and biochemically. The patient was a 44-yr-old man who presented with shortness of breath and a sensation of pressure of the chest. Cytology of the bronchial washings and sputum established the diagnosis of adenocarcinoma. The patient died of respiratory failure after 125 days. Ultrastructurally, there were numerous electron-dense granules in the cytoplasm of most tumor cells, in the apical region; they had a single limiting membrane associated with a clear zone just beneath it. Circular, lamellar, and annulate structures, which closely resembled those observed within zymogen granules of the salivary glands in postnatal mice and rats, were sometimes seen within these granules. These granules are suggested to be identical to a postnatal or immature form of zymogen granules in salivary glands. Biochemical analysis indicated that the amylases obtained from the tumor tissue were composed of sialic acid-containing glycoprotein, which is not found in normal amylases. Since the tumor could produce amylase, mucin, and probably osmiophilic lamellar bodies, it is suggested that the basal cells of the bronchus, especially of a bronchiole, are the precursors of this amylase-producing cancer. (21 refs.)

77-5300 **Questionable Relation of Aryl Hydrocarbon Hydroxylase to Lung-Cancer Risk.** (Eng) Paigen, B. (Dept. Molecular Biology, Roswell Park Memorial Inst., Buffalo, NY 14263); Gurtoo, H. L.; Minowada, J.; Houten, L.; Vincent, R.; Paigen, K.; Parker, N. B.; Ward, E.; Hayner, N. T. *N Engl J Med* 297(7): 346-350; 1977.

Differences in aryl hydrocarbon hydroxylase (AHH) inducibility were examined to determine whether there is a genetic relationship between this trait and hereditary susceptibility to lung cancer. Of 12 patients with lung cancer having resectable tumors, AHH activity was within the normal range in half and < normal in the other half. DNA measurements of cell growth indicated that cell growth was about 50% of normal in some of the patients, including the six with low AHH activity. It was concluded that, in these patients, low AHH activity was due to reduced cell growth and protein synthesis in lymphocytes. AHH genotypes were determined in 57 progeny of cancer patients and 57 matched controls. There was no difference between the two populations in either induced AHH activity or basal AHH levels. This finding held for patients with a strong (1 or more relatives affected) history of cancer. It was concluded that lung cancer patients do not possess a high AHH inducibility that can be transmitted to their progeny. (17 refs.)

77-5301 **Malignant Change in a Solitary Hamartoma of the Lung. A Case Report.** (Eng.) Torikata, C. (Dept. Pathology, Keio Univ. Sch. Medicine, Shinano-machi 35, Shinjuku-ku, Tokyo, Japan); Ishiwata, K.; Fukai, S. *Acta Pathol Jpn* 27(4): 541-546; 1977.

The case of an anaplastic carcinoma arising in a solitary hamartoma of the lung in a 36-yr-old woman is reported. A 3-yr follow-up revealed no other primary tumors or metastases. This case indicates the possibility of malignant change in a hamartoma. (11 refs.)

77-5302 **Disseminated Lipogranulomatosis of Farber. Anatomoclinical and Ultrastructural Studies of Two Familial Observations.** (Fre.) Rivel, J. (Centre Abadie, 89, rue des Sablieres, 33000 Bordeaux, France); Vital, C.; Battin, J.; Heheunstre, J. P.; Leger, H. *Arch Anat Cytol Path* 25(1): 37-42; 1977.

Two fatal cases of disseminated lipogranulosis of Farber occurred in a brother and sister who presented with respiratory difficulties associated with sc and periarticular nodules. At autopsy, the lungs showed marked abnormalities; there were interalveolar nodules in which histiocytes with clear cytoplasm were frequently found. (26 refs.)

77-5303 **Amoeboid Movement Configuration in Tumour Cells of Bone Marrow Smears from Patients with Leukaemia. Incidence and Significance.** (Eng.) Sjogren, U. (Dept. Internal Medicine, Univ. Hosp. Lund, Lund, Sweden); Norberg, B.; Rydgren, L. *Acta Med Scand* 201(4): 381-386; 1977.

The incidence of ameboid movement configuration (AMC), a cell shape suggestive of active locomotion at the moment of fixation, was studied in bone marrow smears from leukemia patients at the time of diagnosis, prior to any treatment. In eight patients with chronic myeloid leukemia (CML), five with acute lymphoblastic (ALL), and nine with chronic lymphocytic leukemia (CLL), incidences of AMC were similar to those found in healthy donors. In contrast, there was a strong positive correlation between AMC incidence and length of survival in 13 patients with either acute myeloblastic (AML) or acute myelomonocytic leukemia (AMML). Further examination of two other populations of 9 nontreated and 19 treated AML-AMML patients also revealed AMC values with a positive skew distribution, in spite of treatment differences. These results suggest that AMC in AML may be due to an immune response of the patient against his own tumor cells. (14 refs.)

77-5304 **Case Records of the Massachusetts General Hospital. Case 31-1977.** (Eng) Winkler, G. F. (Massachusetts General Hosp., Boston, MA); Roberson, G. H.; Shahani, B. T.; Kirshner, H. S.; Scully, R. E.; Schoolnik, G. A.; Bhan, A. K.; Bloch, K. J.; Richardson, E. P.; Samuels, M. A. *N Engl J Med* 297(5): 266-274; 1977.

The case report of a 50-yr-old man who was admitted with respiratory distress is presented in detail. The tentative diagnoses were multiple myeloma, with polyneuropathy of axonal degeneration type, and/or embolic infarction in territory of left middle cerebral artery, secondary to rheumatic carditis. The possibility of a second primary neoplasm in patients with multiple myeloma, possibly due to disordered immune surveillance, was mentioned, but a second primary neoplasm was not evident in this case. The patient died which allowed the following anatomical diagnoses: multiple myeloma, with involvement of bones, skeletal muscle (psoas), lymph nodes (mesenteric, celiac, and para-aortic), spleen, kidneys, liver, parietal pleura and meninges; paraneoplastic motor neuropathy; glomerulonephritis, unclassifed, consistent with immune-complex pathogenesis. (17 refs.)

77-5305 **Disseminated Atypical Tuberculosis Antedating the Clinical Onset of Neoplasia.** (Eng) DiBella, N. J. (Hematology-Oncology Service, Fitzsimons Army Medical Center, Denver, CO 80240); Buchanan, B. D.; Koontz, C. H. *Cancer* 40(3): 1276-1279; 1977.

The case histories are presented of two men, aged 35 and 27 yr, who developed acute granulocytic leukemia and Hodgkin's disease, respectively, following disseminated atypical tuberculosis. In each case, the tuberculosis predated the neoplasia by 4 to 5 yr. Both patients exhibited hematological abnormalities in the course of their illness: the first was leukopenic and anemic 2 hr prior to a *Mycobacterium kansasii* infection, while the second was pancytopenic throughout his illness. Both patients also exhibited defective cellular immunity, although this could have been due to treatment in the first patient. Since both disseminated atypical mycobacteriosis and neoplasia are likely to develop in a patient with impaired cellular immunity or other defective host responses, it is suggested that the same factors may have predisposed the patients to the development of both conditions. (17 refs.)

77-5306 **Development of Chronic Myelocytic Leukemia During the Course of Acute Lymphocytic Leukemia in an Adult.** (Eng) Fisher, B. L. (Div. Hematology, Dept. Medicine, Univ. Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284); Lyons, R. M.; Sears, D. A. *Am J Hematol* 2(3): 291-297; 1977.

A case report is given of a 59-yr-old man who initially presented with an acute lymphocytic leukemia (ALL) that responded well to vincristine and prednisone. After a remission of 9 mo, he acquired the clinical and hematologic features of a myeloproliferative disease (chronic myelocytic leukemia), and cytogenetic studies demonstrated the presence of the Philadelphia chromosome. Within 4 mo he again developed ALL and died. This case is an example of the possible close relationship between lymphoproliferative and myeloproliferative disorders. (19 refs.)

77-5307 **Acute Nonlymphocytic Leukemia. A Delayed Complication of Hodgkin's Disease Therapy: Analysis of 109 Cases.** (Eng) Cadman, E. C. (Dept. Internal Medicine, Yale Univ. Sch. Medicine, New Haven, CT 06510); Capizzi, R. L.; Bertino, J. R. *Cancer* 40(3): 1280-1296; 1977.

Data is presented on 69/109 patients who developed acute nonlymphocytic leukemia (ANLL) following therapy for Hodgkin's disease, including four new case histories which are reported. The series contained 28 men and 36 women; sex was not recorded in 13 patients. The age range was 8 to 74 yr with no age recorded for 13 patients. The leukemia was characterized by cytopenia (present a median of 3 mo prior to diagnosis), megaloblastoid marrow, nucleated RBC in the peripheral circulation, random chromosomal aberrations of the bone marrow, and failure to respond to therapy. The leukemia occurred most often in patients who were treated aggressively. The latent period was significantly shorter in those patients receiving intensive radiotherapy (total nodal irradiation), combination chemotherapy, or a combination of the two. The treatment given to each patient is outlined; however, it was not possible to determine which protocol was the most leukemogenic. The interaction between the leukemogenic and immunosuppressive effects induced by therapy and the immunogenetic status of the patient is discussed. (127 refs.)

77-5308 **The Passage of Macrophages Across Lymphatic Walls by Reverse Diapedesis: An Ultrastructural Study.** (Eng.) Carr, I. (Dept. Pathology, Univ. Saskatchewan, Saskatoon, Saskatchewan S7N OWO, Canada). *J Reticuloendothel Soc* 21(6): 397-402; 1977.

Transmission electron microscopy was used to study the migration of macrophages into lymphatic vessels in granulomas induced in the foodtpads of C3H mice by injection of BCG and Freunds adjuvant. This migration was rare, occurring less often than once in 25 mm^3 of tissue. It occurred by a process of active migration between lymphatic endothelial cells (reverse diapedesis), a process similar to that in the invasion of lymphatic vessels in lymphatic metastasis of tumors. (10 refs.)

77-5309 **Correlation Between Clinical and Anatomical Features of CNS Involvement in Children with Leukemia.** (Ger.) Hrodek, O. (II Kinderklinik der Karls-Universitat, V uvalu 84, 15006 Prague 5-Motol, Czechoslovakia); Hyniova, H.; Svaty, J.; Karpenko, A. *Folia Haematol (Leipz)* 104(1): 48-56; 1977.

Clinical and anatomical findings of CNS involvement in 76 untreated children with acute leukemia (54 with the nonmyeloid form) were compared with those of children who received prophylactic radiotherapy and/or intrathecal methotrexate. Seventeen children showed overt clinical symptoms of CNS involvement, which included intracranial pressure, meningitis, seizures, paralysis, and hypothalamic syndrome. Pathological findings included meningeal infiltrations, perivascular brain infiltration, subependymal infiltration, meningitis, and brain abscess. The av survival time of this group was 17.2 mo. Another group of 17 children (10 with the nonmyeloid form) who had terminal clinical symptoms of CNS involvement (av survival time 11.7 mo) presented with clouded consciousness, coma, and seizures. Autopsies showed a predominance of massive hemorrhaging; two patients showed cerebral purpura, one subarachnoidal hemorrhaging. Five had leukemic infiltrates and two had edema. Overall, 42 children presented with no clinical symptoms and survived an av of 13.2 mo. However, pathology revealed leukemic infiltrates in 12 and subependymal infiltrates in 3. (8 refs.)

77-5310 **Familial Leukemia and Inherited Chromosomal Aberration.** (Eng) Cervenka, J. (Div. Oral Pathology, Sch. Dentistry, Univ. Minnesota 16-206 HS Unit A, Minneapolis, MN 55455); Anderson, R. S.; Nesbit, M. E.; Krivit, W. *Int J Cancer* 19(6): 783-788; 1977.

Chromosomal analyses were performed on members of a family in which two cases of childhood leukemia occurred. The analyses were performed on three occasions, 9 mo apart. In unaffected first-degree relatives, a high frequency of tetra radial figures was found: in parents 1:243 mitoses, and in all first-degree relatives 1:328 mitoses. The rate of chromosomal breakage was elevated in the father (6.16), mother (4.01), and one sister (4.07), compared to matched controls. No abnormalities were reported after G-band and C-banding karyotyping of chromosomes from relatives of the leukemic victims. A possible relationship between the increased incidence of chromatid exchange figures and an increased tendency to leukemia in this particular family was suggested. (26 refs.)

77-5311 **Chromosomes and Causation of Human Cancer and Leukemia. XXIII. Near-Haploidy in Acute Leukemia.** (Eng) Oshimura, M. (Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263); Freeman, A. I.; Sandberg, A. A. *Cancer* 40(3): 1143-1148; 1977.

The case of a 12-yr-old girl with acute lymphoblastic leukemia (ALL) is presented. Karyotypic analysis of a bone marrow aspirate following admission revealed a modal chromosome number of 54 (72.4% of the cells), but 19.5% of the cells had 27 chromosomes. Except for numbers 10, 14, 18 and 21, all cells had only one chromosome of each pair. No normal cells were found. The number 7 chromosome had an additional segment from an unknown chromosome on the distal end of the short arm. The cells with 54 chromosomes were an exact duplication of those cells with 27 chromosomes. Cells obtained in complete remission were all normal. Cells obtained in partial relapse were either normal or had 27 chromosomes, and the number 7 was normal; it appeared that the abnormal number 7 chromosome was replaced by a normal chromosome after therapy. The numbers of large and small lymphoblasts noted cytologically corresponded to the number of cells with 54 and 27 chromosomes, respectively. These findings are discussed and compared to a previously reported case. (11 refs.)

77-5312 **Chromosomes and Causation of Human Cancer and Leukemia. XXIV. Unusual and Complex Ph^1 Translocations and Their Clinical Significance.** (Eng) Sonta, S. (Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263); Sandberg, A. A. *Blood* 50(4): 691-697; 1977.

Karyotypes and clinical data from 30 patients were examined to determine whether chronic myelocytic leukemia (CML) patients with unusual or complex Ph^1 translocations have a different clinical, hematologic and survival picture than the CML patients with the standard translocation. Unusual translocations are defined as those in which the deleted part of chromosome 22 is translocated to a chromosome other than 9; usually number 9, and at least one other. There were 14 unusual translocations involving chromosome numbers 2 (2), 6, 9 (short arm), 11 (2), 13, 14, 16, 17, 19 (2), 21 and 22. The chromosomes involved in the 16 complex translocations were 3, 4, 5, 6 (2), 7 (2), 8, 9 (14), 10 (2), 11 (2), 13 (2), 14, 15 (2), 17, 19, 21, and 22. In no case was the sex chromosome involved. When chromosome 9 was involved, the break was usually at band 934. The age, clinical data, laboratory findings, and survival of these patients did not differ significantly from patients with the standard translocation. However, survival was better in patients with some sort of Ph^1 translocation than Ph^1-negative CML patients. (28 refs.)

77-5313 **Cytogenetic Studies in L$_2$C Leukemia.** (Eng.) Whang-Peng, J. (Medicine Branch, NCI, NIH, Bethesda, MD 20014). *Fed Proc* 36(9): 2255-2259; 1977.

Discrepancies concerning the immunogenicity of L$_2$C leukemic cells in syngeneic hosts and their proliferation in allogeneic animals led to this cytogenetic study. Karyotyping and G-banding of normal guinea pig cells and of four L$_2$C cell lines (GH-L$_2$C, EN-L$_2$C, BZ-L*C, and Lg-L$_2$C) revealed several differences among them. Normal guinea pig cells have 64 chromosomes: 31 pairs of autosomes and 1 pair of sex chromosomes. All four L$_2$C lines had near diploid chromosomes numbers, ranging from 60 to 66. With chromosomes numbered according to size and shape, the short arm designated as "p" and the long arm as "q" and using "+" for addition and "-" for deletion, the following abnormalities were noted: (1) in the LG-L$_2$C line, all cells had the markers M1 and M2 and deletions 2p-, 3p-, and 3q-; 40% of the cells had 1p+, and 45% of the cells had M3; (2) in GH-L$_2$C, all cells had M1, 2q-, XXX, and 3q-; (3) in BZ-L*C, all cells contained M1, 2q-, XX, and 3p-; and (4) in EN-L$_2$C all cells contained M1, XX, and 3p-. M1 was a metacentric marker believed to be 2p translocated to 12q. M2 may represent 18p+q+, but M3 is a minute chromosome. These results suggest a genetic basis for the differences in immunogenicity, particularly in reference to the C$_3$ receptors, but they were not totally consistent. (16 refs.)

77-5314 **Cytogenetic Evidence of Clonal Evolution in 5q- Anemia.** (Eng.) Verhest, A. (Departement de Cytogenetique, Institut Jules Bordet, Centre des Tumeurs, Universite Libre de Bruxelles, Brussels, Beligum); Lustman, F.; Wittek, M.; Van Schoubroeck, F.; Naets, J. P. *Biomedicine [Express]* 27(6): 211-212; 1977.

Case reports of two patients with a 5q- marker of the hematologic entity are presented. In one of these patients, refractory anemia and partial myelofibrosis underwent transformation into acute myelomonocytic leukemia with clonal chromosomal evolution. The other patient showed no signs of leukemic transformation. (8 refs.)

77-5315 **Chromosomes and Causation of Human Cancer and Leukemia. XX. Banding Patterns of Primary Tumors.** (Eng.) Sonta, S. (Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263) Oshimura, M.; Evans, J. T.; Sandberg, A. A. *J. Natl Cancer Inst* 58(1): 49-59; 1977.

Banding techniques were used to study the chromosomes of primary tumors from 16 patients with various types of cancer. The initial analysis with conventional Giemsa staining revealed chromosome abnormalities in 13/16 tumors. Eleven of these 13 tumors and 2/3 with normal karyotypes were reexamined with Q-, G-, and C-banding techniques. The two tumors with conventionally stained normal karyotypes were found to have no abnormalities. Nine of the tumors were characterized by numerical changes only and four by both numerical and structural abnormalities. In five tumors, the numerical changes consisted of extra chromosomes 5, 8, 11, 13, and 21. The primary tumors had hyperdiploid modes; only four contained marker chromosomes, as opposed to the high frequency of markers in metastatic cancer cells and the presence of high ploidy (near-triploidy or near-tetraploidy). The data suggest that the karyotype changes in primary cancers are primarily numerical (hyperploidy). (26 refs.)

77-5316 **Familial Monoclonal Gammopathies: Preliminary Results of a Prospective Study.** (Fre.) Youinou, P. (Clinique Medicale Harvier, CHU, 29279 Brest, France); Le Goff, P.; Saleun, J.-P.; Fauchier, C.; Le Menn, G. *Sem Hop Paris* 53(22-23): 1367-1368; 1977.

To evaluate the possibility of genetic predisposition for monoclonal gammopathies (MG), a prospective study was made in (a) 10,797 presumably healthy subjects and (b) 172 related subjects, 37 of whom were known to have diseases [Kahler's disease (24), Waldenstrom's macroglobulinemia (7), and various MG (6)]. Rheumatoid factor (RF) was determined in 80 of the healthy subjects, anti-DNA antibodies in 85 others. Paraproteins were detected in (a) 141 of the healthy subjects and (b) 10 members of four families: kappa IgG or IgM, RF, and/or anti-DNA were detected in these family members. In conclusion, there may be a genetic predisposition for MG or a relation between MG and immunological disorders ($p < 0.01$). (6 refs.)

77-5317 **Familial Adenocarcinomatosis Across Four Generations.** (Fre) Dubosson, J. D. (Institut de genetique medicale, 8, chemin Thury, CH-1206 Geneva, Switzerland); Klein, D.; Pettavel, J.; Rey, C. D. *Schweiz Med Wochenschr* 107(25): 875-881; 1977.

Familial adenocarcinomatosis was diagnosed in 22/79 persons from four generations, 21 from the first three generations (16 men, 5 women) but only 1 from the fourth generation (21-yr-old woman). The transmission was autosomal dominant, and there was a significant predilection for the male sex (16/22 cases). Overall, 27 malignant tumors were found either at operation, histological examination, or at autopsy (1 case). Of the 27 tumors, 22 were adenocarcinomas (AD), 16 of which localized in the colon. Other tumors included duodenal AD (1), gastric AD (2), rectal AD (1), papillary carcinoma of the ovary (1), osseous sarcoma (1), cutaneous fibrosarcoma (1), multiform glioblastoma of the basal nuclei of the brain (1), basocellular epithelioma (1), cerebral metastasis from AD (1), and a tumor invading the biliary tract (1). Multiple tumors occurred in three members of the family, and colonic AD was associated with one or two polyps in three others. In the first generation, the tumor occurred at an av age of 57 yr, compared with 52.6 and 41.6 yr for the second and third generations, respectively. Of the 22 patients with AD, 6 died of their disease. (37 refs.)

77-5318 **Characterization of a New Continuous Cell Line Derived from a Human Retinoblastoma.** (Eng.) McFall, R. C. (Wills Eye Res. Inst., Philadelphia, PA 19130); Sery, T. W.; Makadon, M. *Cancer Res* 37(4): 1003-1010; 1977.

WERI-Rb1, a new continuous cell line, was characterized on the basis of morphology, growth, tumorigenicity and cytogenetics, and compared with Y79, another human retinoblastoma cell line. The lines were similar, except that only Y79 could be cloned in soft agar. WERI-Rb1 showed a stable, modal chromosome number of 46 with at least 5 markers present in every cell. (24 refs.)

77-5319 **Cytological and Cytophotometric Studies on DMBA-induced Changes of the Conjunctival Epithelium in Syrian Golden Hamsters.** (Eng) Haag, D. (Universiat Heidelberg, Institut fur vergleichende und experimentelle Pathologie, D-6900 Heidelberg, W. Germany); Schlieter, F.; Ehemann, V.; Goerttler, K. *Z Krebsforsch* 89(2): 201-214; 1977.

Changes induced in the conjunctival epithelium of 30 female Syrian golden hamsters receiving 1 drop/day of a 1% solution of 7,12-dimethylbenz(a)anthracene (DMBA) for 6 mo are presented. Smears of scraped conjunctival and corneal cells were obtained weekly and stained. Large numbers of inflammatory cells were present by day 11; the smear could be characterized by acute inflammation and hyperplasia. After 4 wk, the composition of the cells was almost normal, but the smears contained more cells than controls. After 2 mo, cells with degenerative changes and signs of cell decomposition were evident. The number of cells with signs of malignancy increased from the second to the fifth months, but no invasive carcinomas were observed until the sixth mo. Only 1/20 animals developed a carcinoma in situ of the cornea after 5 mo, but all animals developed carcinomas of organs such as the eyelid, esophagus, forestomach, and stomach. Since most animals died between the 6th and 12th months, observations could not be continued. Although there were few chromatin changes, nuclear volume increased up to 40%. Correspondingly, after 2 mo, nuclear DNA values in the diploid-tetraploid range were noted. These aberrations increased with DMBA exposure. (38 refs.)

See also:

* (Rev.): 77-4808, 77-4809, 77-4826, 77-4830, 77-4839, 77-4846, 77-4851, 77-4854, 77-4855, 77-4856, 77-4857, 77-4859, 77-4860, 77-4861, 77-4862, 77-4863, 77-4864, 77-4865, 77-4866, 77-4867, 77-4868, 77-4869.
* (Chem.): 77-4924, 77-4927, 77-4930, 77-4934, 77-4937. 77-4943, 77-4945, 77-4959, 77-4960, 77-4973, 77-4978, 77-4985, 77-4990, 77-4992, 77-4996.
* (Phys.): 77-5021, 77-5024, 77-5027, 77-5028, 77-5031, 77-5032, 77-5040.
* (Viral): 77-5112, 77-5149, 77-5150, 77-5151, 77-5154, 77-5174.
* (Immun.): 77-5175, 77-5183, 77-5194, 77-5201, 77-5202, 77-5204, 77-5205, 77-5207, 77-5208, 77-5217, 77-5219, 77-5220, 77-5243
* (Epid.-Biom.): 77-5338, 77-5343.

77-5320 **The Probability of Developing Cancer.** (Eng.) Zdeb, M. S. (Office Biostatistics, New York State Dept. Health, Tower Building, Empire State Plaza, Albany, NY 12237). *Am J Epidemiol* 106(1): 6-16; 1977.

Data on cancer morbidity for 1969-1971 in upstate New York and 1970 life-table data were used to estimate the current probability of developing cancer and the current probabilities compared with those estimated for 1940, 1950, and 1959. The number of cancer cases expected to occur in the life-table population was calculated by multiplying the population by the appropriate age-specific cancer-incidence rate; this was done for each 5-yr age group. The number of cancer cases expected to occur among the life-table population from birth through the last age interval (85+ yr) is the sum of all the age-specific totals. It was assumed that life-table deaths and the probability of dying in a specific age interval could be divided into cancer-related and non-cancer-related deaths and probabilities by using the ratio of the cancer death rate to the death rate from all causes prevailing in the population. The current probabilities at birth of developing cancer, assuming a life span of 85+ yr, are 27.13 cases/100 for men and 27.75/100 for women. For men, the three leading sites (lung, prostate, and large intestine) account for 46% of the total probability. For women, the three leading sites (breast, large intestine, and corpus uteri) comprise 45% of the total probability. The only sites among the top 10 to have declined over the period 1950-1960-1970 are stomach for both sexes and cervix uteri for women. If the cutoff point for determining probabilities at birth is age 65, the overall probability of developing cancer decreases dramatically: for men from 27.13 to 9.96 cases/100 and for females from 27.85 to 11.55. The data can also be used to estimate current probabilities of developing cancer at various ages. (4 refs.)

77-5321 **Age Incidence Curves for Cancer.** (Eng.) Watson, G. S. (Dept. Statistics, Princeton Univ., Princeton, NJ 08540) *Proc Natl Acad Sci USA* 74(4): 1341-1342; 1977.

The fact that age incidence curves for carcinomas tend to be linear on doubly logarithmic graphs has been used to support the somatic mutation hypothesis. In its simplest form, it supposes that a stem cell becomes cancerous when each of n specified loci have mutated. If this cell continues to divide and λ ,...,λn are the time rates of mutation in the immortal line of the n loci, the cell will be cancerous at time t or less with probability $P(t)$. An equation is given by which the time to cancer for a tissue can be approximated; it follows a Weibull distribution without restriction to small values of t. The equation can be obtained with stochastic models that are consistent with the epigenetic mechanism, when reversible cellular changes are programmed to occur ramdonly. It can be obtained with reversible models. The linear relation can also be used to assess the risk due to an additional carcinogen at low constant dosage. (10 refs.)

77-5322 **Territorial Differences in Tumor Incidence. Geographic Analysis of Data from a Cancer Register.** (Fre.) Panero, M. (Registro dei Tumori per il Piemonte e la Valle D'Aosta, Turin, Italy). *Med Biol Environ* 4(1): 7-9; 1977.

For each municipality of the Piedmont district, the actual number of tumors registered was compared with the anticipated number based on tumor incidence in the district as a whole. The municipalities were divided into three groups: (1) those with a> 10% (higher than expected) incidence of tumors, (2) those with the expected incidence, and (3) those with a ≤ 10% tumor incidence. Data were analyzed further on the basis of sex. The municipalities with a> 10% incidence tended to have a greater population density, whereas municipalities with ≤ 10% incidence were mountainous or rural. Variations could be attributed to real differences in cancer morbidity, differences in case registration, or errors in determining the place of residence. (no refs.)

77-5323 **Trends in Cancer Incidence in Allegheny County, Pennsylvania, 1937-71.** (Eng) Emes, J. J. (325 Parran Hall, Graduate Sch. Public Health, Univ. Pittsburgh, Pittsburgh, PA 15261); Redmond, C. K.; Jarmolowski, N. *Public Health Rep* 92(4): 365-373; 1977.

Cancer incidence rates by race, sex, and site for Allegheny County for 1969-71 were presented and compared with earlier rates (1937, 1947, and 1957-58). For all sites combined, the male rate was substantially higher than the female rate, and the black male rate much higher than the white male rate. The largest annual increase in both sexes was seen for cancers of the lung, bronchus, and trachea. Stomach cancer incidence decreased, but there was a slow steady rise in breast cancer, prostate cancer, and cancer of the esophagus and pancreas. Possible etiological factors (eg, air pollution, smoking, diet) are discussed in relation to the epidemiologic data. (32 refs.)

77-5324 **Occurrence and Trend of Lung Cancer in the Population of the Second District of Prague.**

(Cze.) Macholda, F. (No affiliation given); Mericka, O.; Vackova, H. *Cas Lek Cesk* 116(7): 222; 1977.

Epidemiological data are presented concerning lung cancer in the Second District of Prague for the period 1960-1975. This district has about 100,000 inhabitants. The cumulative mortality during the investigation period was 21,815, 5,589 of whom died of malignant neoplasms. Primary lung cancer was the cause of death in 970 cases. The lung cancer mortality rate was 47.3/100,000 in 1960 and 96/100,000 in 1975. Data on 465 lung cancer patients treated at a clinic show that epidermoid cancer accounted for 39.2%, anaplastic undifferentiated cancer for 22.3%, small-cell carcinoma for 14.2%, adenocarcinoma for 2%, and other types for 22.3%. (no refs.)

77-5325 **Cancer Incidence in the Endemic Nephropathy Region of Vratsa, Bulgaria.** (Bul.) Chernozemski, I. (Medical Acad., Inst. Oncology, Bulgaria) Stoianov, I.; Petkova-Bocharova, T.; Nikolov, I.; Draganov, I.; Stoichev, I. *Onkologiia* 14(1): 4-13; 1977.

Cancer incidence in a region with endemic nephropathy (EN) was studied over a 9-yr period. Twenty-seven villages with an av annual population of 26,801 were divided into four groups according to the frequency of EN: high (A), medium (B), low (C), and none (D). Of 1,519 cases of malignant tumor, 326 were eliminated because of a lack of medical history. Of the remainder, 657 were in Group A and B and 426 in C and D. Urinary tract tumors (UTT) were found in 207 patients (177 in the Groups A and B and 30 in C and D). Differences among other tumor sites were statistically insignificant. In hyperendemic villages, the rate of UTT/100,000 population (grouped according to age) was 104 men and 89 women. In villages with high and moderate incidences of EN, UTT were the most common neoplasms. They accounted for 25% of all tumor sites for men and 30% for women. The rate of UTT in the most affected village was 231.5/100,000 for women and 185/100,000 for men. Tumors of the ureter and renal pelvis were most common in women between 50 and 60 yr of age. UTT were often multiple, and 89% of them originated in the uroepithelium. There was a correlation between UTT and EN in terms of geographic distribution and other epidemiologic characteristics, such as age and sex. (21 refs.)

77-5326 **Clustering of Mycosis Fungoides in the County of Vasternorrland, Sweden.** (Swe.) Gip, L. (Hudkliniken, Sundsvalls Sjukhus, Sundsvall, Sweden); Nilsson, E. *Lakartidningen* 74(12): 1174-1176; 1977.

Statistical analysis of epidemiological data on histologically confirmed cases of mycosis fungoides showed a clustering of this disease in the county of Vasternorrland, Sweden, during the period 1959-1975. The incidence, far above the countrywide av, was 4.4 cases/1,000,000 inhabitants/year vs 1.8 cases for Sweden as a whole. A total of 31 cases was recorded from 1960 to 1975; the male: female ratio was 21:10. The age range was 20-80 yr, but most patients were in the range 51-60 yr. Fourteen patients lived in towns, 8 in villages, and 9 in sparsely populated areas. Most of the male patients were forest and farm workers, and four of the female patients were wives of these workers. (19 refs.)

77-5327 **Studies on Correlation of Skin Cancer and Tobacco Growing in Szabolcs-Szatmar County, Hungary.** (Hun.) Szego, L. (Szabolcs-Szatmar megyei Tanacs "Josa Andras" Korhaza, Borosztaly, Nyiregyhaza, Hungary); Jarmy, J.; Vargha, L. G. *Magy Onkol* 21(1): 51-59; 1977.

Epidemiological data are presented on skin cancer incidence and morbidity in Szabolcs-Szatmar County, Hungary, which accounts for 40% of the country's tobacco production and where 80% of the farm workers are engaged in tobacco growing. Of all the counties of Hungary, the incidence of skin cancer was highest in Szabolcs-Szatmar county. From 1965 to 1968, skin cancer patients accounted for 9.5% of all new cases of skin disease in the county. From 1959 to 1968, skin cancer was diagnosed in 557 men and in 494 women; 91.2% of the men and 86.4% of the women were agricultural workers. A very close correlation was found between the geographic distribution of tobacco growing and that of the skin cancer patients within the county. Basal cell carcinoma, squamous cell carcinoma, and spindle cell carcinoma were the most common types found. The skin cancer was localized to the head and neck region in 90% and to the exposed parts of the limbs in 5% of all cases. The findings indicate that certain substances originating in tobacco plants may play a role in the genesis of skin cancer. (24 refs.)

77-5328 **A Study of Lung Cancer in Relation to Bidi Smoking in Different Religious Communities in Bombay.** (Eng.) Notani, P. N. (Tata Memorial Center, Parel, Bombay-400 012, India); Rao, D. N.; Sirsat, M. V.; Sanghvi, L. D. *Indian J Cancer* 14(2): 115-121; 1977.

A retrospective study was conducted of 683 male lung cancer patients and 1,279 male noncancer patients seen in one Indian hospital betwee 1963 and 1971 to examine geographic/religious differences in smoking habits in relation to lung cancer. Compared with nonsmokers, the estimate of relative risk for bidi smokers [a relatively small cigarette containing only 0.25-0.50 g tobacco flakes wrapped in a piece of dried temburni (*Diospyros melanoxylon*) leaf] and cigarette smokers was 3.38 and 2.36, respectively, Bidi smoking is much more prevalent in India and bidi smoke has a higher level of toxic agents and carcinogenic hydrocarbons than cigarette smoke, yet the overall incidence of lung cancer in India is much lower than that in Western countries. The coarse variety of bidi tobacco plus the uneven burning of the bidis may lead to an internal dispersal of smoke particles that would have greater impact on sites further up the respiratory tract, before the lungs are reached. The estimate of relative risk of bidi smokers for oropharyngeal cancer was 10.37, compared to those who neither smoke nor chew betel leaf, indicating that the max impact of bidi smoke is on the oropharynx. In every category of bidi smoking the Muslims had the highest relative risk, although they did not smoke more or for a longer duration than the Hindu smokers. These differences indicate the presence of other, as yet unidentified, modifying factors. (14 refs.)

77-5329 **Ohio Drinking Water Source and Cancer Rates.** (Eng) Kuzma, R. J. (Dept. Environmental Health, Div. Epidemiology and Biostatistics, Univ. Cincinnati, Cincinnati, OH 45267); Kuzma, C. M.; Buncher, C. R. *Am J Publ Health* 67(8): 725-729; 1977.

Analysis of covariance was used to compare cancer mortality patterns in 88 Ohio counties that were classified as either ground water (GWC) or surface water counties (SWC), based on the source of drinking water used by most residents. Forty-two counties were classified as GWC and 46 as SWC. The cancer mortality rates for white men were significantly higher in SWC than in GWC (5% higher for all cancers and 19% and 18% higher for stomach and bladder cancers, respectively). The stomach cancer mortality rate for white women was significantly higher ($p = 0.038$) in SWC than in GWC. These differences were not attributable to urbanization, median income, population size, or agricultural or manufacturing activity. It is suggested that the surface drinking water supplies contained substances that can cause cancer. (12 refs.)

77-5330 **Unusual Mortality Experience of Printing Pressmen.** (Eng) Lloyd, J. W. (United Steelworkers America, AFL-CIO, CLC, Washington, DC); Decoufle, P.; Salvin, L. G. *J Occup Med* 19(8): 543-550; 1977.

Causes of death for 2,604 members of a union representing printing pressman who died during 1966-1968 were examined to identify disease conditions occurring with unusual frequency that might indicate exposure to toxic susbtances in the work environment. Comparisons were made with the mortality experience of US white men in 1967. Newspaper pressmen showed a significant excess (7 cases) of cancer of the buccal cavity and pharynx that was confined to the early and middle working years (av age at death was 46.7 yr). There was also a significant excess of cancer mortality in these men before age 45; the sites were tongue, 2; stomach, 1; large intestine, 2; pancreas, 1; sinus, 1; lung, 1; and leukemia, 1. Significant excesses in deaths from pancreatic cancer at ages 20-54 and rectal cancer at ages > 65 were observed among commercial pressmen. A small nonsignificant increase in cancer of the lung and bronchus was noted for both newspaper and commercial pressmen. Mortality from leukemia was slightly greater than expected among newspaper pressmen but not among commercial pressmen. The observation of excess mortality before age 45 among newspaper pressmen suggests exposure to a particularly potent carcinogen. (15 refs.)

77-5331 **Mortality by Cause Among Stationary Engineers and Stationary Firemen.** (Eng) Decoufle, P. (Environmental Epidemiology Branch, NCI, Bethesda, MD 20014); Lloyd, J. W.; Salvin, L. G. *J Occup Med* 19(10): 679-682; 1977.

Mortality statistics were examined for 1,113 stationary engineers and firemen to determine and excess risks in the working environment. Cancer of the buccal cavity and pharynx were found at twice the expected rate. The same order of increased risk of these cancers was observed in the Northeast and Midwest; no deaths were noted in the South and only one in the West. There was a two-fold excess of rectal cancers consistent for all regions except the South. Insignificant increases in lung cancer mortality were noted in all regions. The excess for buccal cavity and pharyngeal cancer was confined to the older ages (primarily after age 65) while rectal cancer was excessive at all ages. The greatest excess of lung cancer occurred after age 65. Mortality statistics for heart disease and nonmalignant respiratory disease are also presented. It is suggested that these cancer statistics be considered in terms of potential exposure to occupational carcinogens such as hydrazines. (20 refs.)

77-5332 **Possible Increased Risk of Lung Cancer among Beauticians.** (Eng.) Garfinkel, J. (Dept. Biomedical and Environmental Health Sciences, Sch. Public Health, Univ. California, Berkeley, CA 94720); Selvin, S.; Brown, S. M. *J Natl Cancer Inst* 58(1): 141-143; 1977.

Death certificates of residents of Alameda County, California (1958-1962) were examined to determine the risk of cancer among beauticians. Twenty-four beauticians were found among 3,460 adult women who died with cancer; 4 were found in a sample of 1,000 women who died from causes other than cancer. The case and control certificates were atched for age and race. The resulting odds ratio (ie, approx elative risk of a cancer death) was slightly elevated (1.73) ut was not statistically significant. Although a possible increase in the risk of cancer was found for several organ sites, he increase in risk for lung cancer was most striking. Analsis of pairs of death certificates, in which female controls ying of causes other than cancer were matched to female ng cancer cases for age, race, and date of death, yielded an dds ratio of 6.0. This finding suggested that the risk of lung ancer may be substantially increased among female beautiians. (11 refs.)

7-5333 **Occupational Hazards for Operating Room-based Physicians. Analysis of Data from the Jnited States and the United Kingdom.** (Eng.) Spence, A. A. Western Infirmary, Glasgow, Scotland) Cohen, E. N.; rown, B. W.; Knill-Jones, R. P.; Himmelberger, D. U. *AMA* 238(9): 955-959; 1977.

ata from recent surveys reaffirm the increased incidence of pontaneous abortion among female physicians working in he operating room and an increase of congenital abnormalies in their offspring. Male anesthetists had an increased incience of hepatic disease and of congenital abnormalities in heir offspring. (10 refs.)

7-5334 **Carcinogenesis in the Laboratory.** (Eng.) Haski, R. (Div. Occupational Health and Radiation Control, Health Commission New South Wales, Joseph St., Lidcombe, NSW 2141, Australia). *Cancer Forum* (11): 406-407; 1977.

n a survey of several laboratories handling carcinogenic subtances or suspected carcinogens, inappropriate procedures were found for identifying compounds, handling and disposng of them, monitoring personnel, and eliminating contamiation. A report in preparation will set forth guidelines for these laboratories. (no refs.)

77-5335 **Thyroid Diseases in Black Patients.** (Eng) Chung, E. B. (Dept. Pathology, Howard Univ. Coll. Medicine, 520 W St. NW, Washington, DC 20059); Rogers, N.; White, J. E. *J Natl Med Assoc* 69(8): 573-577; 1977.

Thyroid diseases in black patients are discussed from an epidemiological point of view. Of 680 patients with abnormal thyroid glands selected for thyroidectomy, 353 were found to have nodular (adenomatous) goiter; 145, diffuse hyperplasia; 77, adenoma; 48, various thyroiditis; 31, carcinoma; and 26, miscellaneous conditions. The ratio of female to male patients was 7:1 (literature value is approx 10:1), which was consistent with the fact that diseases of the thyroid gland are more prevalent among women than men. (22 refs.)

77-5336 **Immunodeficiency-Cancer Registry: 1975 Update.** (Eng.) Spector, B. D. (Dept. Lab. Medicine and Pathology, Univ. Minnesota, Minneapolis, MN 55455). *In: Genetics of Human Cancer.* Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F. (New York: Raven Press): Progress in Cancer Research and Therapy. 3: 339-342; 1977.

Data were collected over a 26-yr period on 205 children and adults who developed cancer subsequent to the diagnosis of a primary immunodeficiency disease. Lymphoreticular tumors predominated; the second most common malignancy was leukemia, followed by epithelial neoplasms, nervous system tumors, and mesenchymal cancers. (3 refs.)

77-5337 **Target Theory Applied to Acute Leukemia in Down's Syndrome and the General Population.** (Eng.) Lubiniecki, A. S. (Life Sciences Div., Meloy Lab., Inc., Springfield, VA 22151). *In: Genetics of Human Cancer.* Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F., eds. (New York: Raven Press): Progress in Cancer Research and Therapy Vol. 3, pp. 83-85; 1977.

Epidemiological data was obtained from several morbidity studies and death certificate studies comparing childhood leukemia mortality in Down's Syndrome (DS) against a general population. These findings were subjected to target theory analysis; and inconsistencies were found, such as the lower frequency of very young (2-3 yr old) leukemic DS patients in the morbidity study when compared to death certificate data. (7 refs.)

77-5338 **Lymphatic Metastasis with Childhood Rhabdomyosarcoma.** (Eng.) Lawrence, W. (Div. Surgical Oncology, Medical Coll. Virginia, Richmond, VA 23298); Hays, D. M.; Moon, T. E. *Cancer* 39(2): 556-559; 1977.

Lymphatic metastasis was assessed in 264 patients (all younger than 21 yr) who were entered into the Intergroup Rhabdomyosarcoma Study from November 1972 to September 1975. There were 43 patients in Group I, 69 in Group II, 95 in Group III, and 57 in Group IV. The most frequent site of origin was the head and neck (96 patients, 19 of whom had their lesion in the orbit), followed by the extremities (61), genitourinary region (61), and trunk (46). The prevalence of lymph node metastases (Group IV patients were excluded) was higher than expected from the extremities (8/46) and the genitourinary region (10/52) with a somewhat lower incidence from the orbit (0/17), other head and neck sites (2/62), and trunk (3/30). These differences in lymphatic metastases had no relationship to age, sex, tumor size, or histologic type. (8 refs.)

77-5339 **Breast Cancer Controversy Continues (2 Letters to Editor).** (Eng.) Frankl, G. (Southern California Permanente Medical Group, Los Angeles, CA); Friedman, A. K. *Am J Roentgenol* 129(4): 758-759; 1977.

A retrospective study revealed that women with a breast tissue parenchymal pattern designated at risk had a twofold higher incidence of breast cancer than those with a pattern not designated at risk. A review of another study, however, revealed that the risk was not as great as had originally been suggested. (8 refs.)

77-5340 **Breast Cancer Incidence According to Weight and Height in Two Cities of the Netherlands and in Aichi Prefecture, Japan.** (Eng) de Waard, F. (Instituut voor sociale genesskunde, Rijksuniversiteit Utrecht, Bijlhouwerstraat 6, Utrecht, 2501, The Netherlands); Cornelis, J. P.; Aoki, K.; Yoshida, M. *Cancer* 40(3): 1269-1275; 1977.

The role of height and wt in the incidence of breast cancer in The Hague and Rotterdam in The Netherlands and the Aichi prefecture in Japan was evaluated. The study was based on a comparison of 1,006 breast cancer patients and 4,201 controls aged 35 to 69 yr. In The Netherlands, it was shown that for women under 60 kg, the incidence of breast cancer did not rise until after menopause. In women $\geq$ 70 kg compared to those $<$ 60 kg, the risk ratio of the former increased from unity at age 40 to slightly under 2 at age 65. A risk ratio of women $\geq$ 165 cm compared with those under 160 cm showed an increase with age up to 1.6 in the oldest age group. A combination of the two groups of data showed that with increase in body size (surface) the incidence of breast cancer rises, a similar association to that seen with wt. The Japanese figures, with adjustments for height using 150 cm and for wt using 50 kg as the dividing lines, showed the same associations. A comparison between the countries suggested that about 50% of the incidence difference could be attributed to differences in height and wt between the two populations. It is suggested that a hormonal factor governing height and wt may be realted to breast cancer development. (12 refs.)

77-5341 **A Case Control Study of Carcinoma of the Ovary.** (Eng) Newhouse, M. L. (TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, Keppel St., London WC1E 7HT, England); Pearson, R. M.; Fullerton, J. M.; Boesen, E. A.; Shannon, H. S. *Br J Prev Soc Med* 31(3): 148-153; 1977.

In an attempt to identify etiological factors, 300 women with carcinoma of the ovary diagnosed at laparotomy and two control groups matched by age were asked to complete a questionnaire. Approx 19% of the cancer patients had not married compared with only 7.6% and 10.3% of control subjects. Also, 38% of the patients had never been pregnant (vs 11% and 20% in controls), and they tended to have smaller families. Significantly fewer patients had mumps, measles, or rubella. Only 81/900 total women in the series used oral contraceptives, 19 patients and 31 subjects in each of the control groups, a statistically significant deficiency. This study did not provide any new definitive epidemiological leads to factors associated with the development of ovarian carcinoma. (13 refs.)

77-5342 **Epidemiology of Endometrial Cancer.** (Eng) Elwood, J. M. (Cancer Control Agency British Columbia, 686 W. Broadway, Vancouver, British Columbia, Canada V5Z 1G1); Cole, P.; Rothman, K. J.; Kaplan, S. D. *J Natl Cancer Inst* 59(4): 1055-1060; 1977.

The relative incidence (RI) of endometrial cancer was investigated based on 440 cases diagnosed from 1965 to mid 1969 and controls from the general population. The av incidence rate was 18.1 (European standard)/ 100,000 women; the incidence rose sharply from ages 40 to 55-59, then gradually declined. Compared to an RI of unity for married nulliparous women (highest risk), the standardized RI (SRI) for married women of parity 1 was 0.6. Increased parity was associated with further reduced risk. Unmarried women had an SRI of 0.8. The decrease in risk with increasing parity was greater for women aged 40 to 59 than for older women. There was no clear association of endometrial cancer with age at first birth. Women who had menarche at $<$ 12 yr had an RI of 1.6. For women over 50, risk rose with increasing menopausal age: women with menopause at 52 had 1.7 times the risk of women with menopause before age 49. Among married women, 26% of the cases and 27% of the controls had a miscarriage or stillbirth; the RI was 1.1. The RI for breast feeding was 1.0 (53% cases and 50% controls). There was a weakly positive association between risk and social class. Obese women also had a risk 1.9 times that of women with normal build. There was an RI of 2.8 for diabetics, an RI of 2.1 for hypertensives and an RI of 1.3 for arthritics. These findings suggest that hormonal activity is an important factor in endometrial cancer. (32 refs.)

77-5343 **Epidemiology of Malignant Bone Tumours.** (Eng) Ott, G. (Evangelisches Krankenhaus, Chir. Abt., Waldstrasse 73, D-5300 Bonn-Bad Godesberg,

W. Germany); Wagner, G. *Z Krebstorsch* 89(3): 231-243; 1977.

The incidence rates; geographical, racial, age, and sex distributions; histological types; and localization within the skeleton of malignant bone tumors are surveyed. Mesenchymal cells represent 82.5% of the mass of the body, but supply only 6% of malignant tumors; in contrast, > 80% of all malignant tumors originate from the epithelial tissue, which accounts for < 20% of the body mass. Epithelial cells are particularly exposed to environmental carcinogens, but the mesenchymal cells can only be reached by penetrating rays or they are endangered by resorbed sarcogenic agents via the body fluids. The preferred sites for sarcomas are in zones of increased cell division; metaphyses with the highest growth rate, such as the distal femur, proximal humerus, and proximal tibia, are predominantly involved. The presarcomatous diseases observed so far are tabulated, along with several physical causative agents. These include trauma, foreign bodies (implants), ionizing radiation (x-rays, radium, thorotrast, peteosthor, radioactive iodine), and homoiotransplants (bone transplants). Iatrogenic sarcomas caused by several of these factors have been described. A uniform classification of bone tumors plus cooperative participation in a bone tumors registry are recommended. (44 refs.)

77-5344 **The Epidemiology of Bladder Cancer. A Second Look.** (Eng) Wynder, E. L. (American Health Foundation, 1370 Ave. of the Americas, New York, NY 10019); Goldsmith, R. *Cancer* 40(3): 1246-1268; 1977.

The epidemiology of bladder cancer is considered based on a case-control study of 574 men and 158 women seen over a 5-yr period, and these results are compared to those from previous investigations. Bladder cancer occurs more in men than in women, except in Egypt, where both sexes are exposed to *Schistosoma hematobium* and the incidence is about equal. Bladder cancer also affects nearly twice as many white men and women as black women. Cigarette smokers of both sexes were at a higher risk than non-smokers. About 50% of the male cases and 33% of the female cases were attributed to cigarette smoking; there was a fairly consistent dose-response relationship for amount and duration of smoking in both sexes. However, no significant differences were observed between the proportions of cases and controls who used pipes, cigars, chewing tobacco or snuff. There was also an excess of bladder cancer in persons with occupational exposure to rubber, chemicals and textiles. An increase in risk with coffee drinking was noted in both sexes; this increase was slightly higher in men and was independent of smoking levels. No relationship was found between alcohol consumption and bladder cancer. No association was found for artificial sweetners. It is suggested that further studies concentrate on metabolic factors since cigarette smoking and occupational exposure did account fully for the observed incidence. (120 refs.)

77-5345 **Two Aspects of the Epidemiology of Bladder Cancer in England and Wales.** (Eng.) Davies, J. M. (Div. Epidemiology, Inst. Cancer Res., Fulham Road, London SW3 6JB, England). *Proc R Soc Med* 70(6): 411-413; 1977.

A review of death certificates in England and Wales indicated that the number of deaths attributed to bladder cancer may be an understatement. A further study of paraplegics indicated that there is probably an excess of bladder cancer among these patients. (2 refs.)

77-5346 **An Epidemiological Study of Esophageal Carcinoma in Oklahoma City Hospitals, 1970-1975 (Meeting Abstract).** (Eng.) Kenya, P. R. (Univ. Oklahoma, Oklahoma City, OK 73190) Asal, N. R. *Am J Epidemiol* 106(3): 240; 1977. (no refs.)

77-5347 **Mortality from Esophageal Cancer in Piedmont, Italy.** (Eng) Pastore, G. (Registro dei Tumori per il Piemonte e la Valle d'Aosta, Turin, Italy); Vigliani, R.; Terracini, B. *Tumori* 63(4): 309-314; 1977.

Mortality from esophageal cancer was investigated in Piedmont, which is located at the border between Italy (where mortality from this cancer is relatively low) and France and Switzerland (where it is relatively high). The age-adjusted yearly mortality rates for 1965-1969 were 4.3 and 0.8/100,000 for men and women, respectively. The rates were similar in the town of Turin, in 23 suburbs, in the nonmetropolitan areas of the province of Turin, and in the other 5 provinces of Piedmont. In both sexes, the rates did not differ from those observed in Italy during 1966-1967, but rates for men were lower than the national rates for France and Switzerland (14.0 and 8.5/100,000/year, respectively). The rates for men were also lower than in the adjacent French departments of Savoie, Haute-Savoie, and Isere (where in 1967-1968 they ranged between 9 and 16). Mortality rates from esophageal cancer in the town of Turin were constant from 1951-1971. During the same period, mortality from laryngeal cancer in men doubled. It is suggested that although some etiological agents (alcohol consumption and tobacco smoking) are common to esophageal and laryngeal cancer, the interplay between these factors is different for the two types of cancer. (16 refs.)

77-5348 **Cancer of the Esophagus in Southern Iran.** (Eng) Sadeghi, A. (Dept. Radiology, Nemazee Hosp., Shiraz, Iran); Behmard, S.; Shafiepoor, H.; Zeighmani, E. *Cancer* 40(2): 841-845; 1977.

An epidemiological study of esophageal cancer in southern

Iran covers the 5-yr period 1969-1973 and is based on hospital records. The minimal yearly incidence of esophageal cancer was 5-10 times higher than the yearly incidence in Connecticut for the age group 15-44. In the age group 50-65+, the observed incidence rates dropped below those of Connecticut. Of the patients whose tumor site was recorded, 11/15 in the 20-34 age group and 13-52 in the 35/49 age group had a tumor in the upper third of the esophagus. The location of the tumor was related to age but not to sex, after taking age into account. The proportion of female esophageal cancer cases was significantly greater than that of the other gastrointestinal tract cancers combined. It appears that the risk in men and women in this region is nearly equal, but risk could conceivably be higher in women (similar to the appearance of the disease in northern Iran). The etiology of the disease in this region is not associated with tobacco smoking and/or alcohol use, since these habits do not correspond with the epidemiology of the disease. Iron-deficiency anemia and prolonged zinc deficiency may be possible etiological factors. (13 refs.)

77-5349 **Oral Cancer in Puerto Rico.** (Eng.) Fischman, S. L. (Dept. Oral Medicine, Sch. Dentistry, State Univ. New York at Buffalo, Buffalo, NY 14214); Martinez, I. *J Surg Oncol* 9(2): 163-169; 1977.

The epidemiology of oral cancer in Puerto Rico is reviewed and compared with analogous data from the continental US. The incidence of oral cancer in Puerto Rico is fourth highest in the world, accounting for 7.2% and 2.5% of all cancers in men and women, respectively, in 1972. (12 refs.)

77-5350 **Epidemiologic Pathology of Gastric Ulcer and Gastric Carcinoma among Japanese in Hawaii.** (Eng.) Stemmermann, G. (Kuakini Medical Center, 347 N. Kuakini St., Honolulu, HI 96817); Haenszel, W.; Locke, F. *J Natl Cancer Inst* 58(1): 13-20; 1977.

A case-control study of 133 Hawaiian Japanese with gastric ulcers indicated that ulcers in the proximal portion of the pyloric antrum have features similar to those of gastric cancer. These ulcers occurred at sites affected most frequently and most severely by intestinal metaplasia; however, the metaplasia tended to be less extensive than that in cancer. Metaplastic mucosa was more vulnerable to the action of pepsin and acid than was normal mucosa. The risk of ulceration increased when a sufficiently large area of the antrum was intestinalized and when the corpus continued to produce significant quantities of these substances. The study showed a strong association between salt intake, ulcer, and metaplasia. Significant but less dramatic associations were demonstrated between metaplasia and the use of traditional Japanese foods and smoking. It remains to be determined whether salt promotes ulceration or is synergistic with a mutagen that causes intestinal metaplasia. (22 refs.)

77-5351 **Alcoholism and Cancers of the Digestive Tract in the Mediterranean Region of France.** (Fre.) Picheral, H.; (Univ. Paul Valery, Montpellier III, France) *Med Biol Environ* 4(1): 26-35; 1976.

Although inhabitants of the Mediterranean region appear more vulnerable to bronchopulmonary cancer, they have a lower incidence of digestive tract tumors compared to the total French population. Records of the Anticancer Center of Montpellier were used to determine the frequency of gastrointestinal tumors compared to tumors in other sites. Gastrointestinal tumors accounted for 27%-31% of all tumors for Mediterraneans compared to 33%-40% for the overall population. When the data were analyzed according to smaller locales (cantons) within the Mediterranean region, the lower incidence of gastrointestinal tumors was found to occur in urban and industrial areas. Alcoholism appears to be related to gastrointestinal tumors, because the Mediterranean wine-growing locales have the highest incidence of alcoholism and cirrhosis of the liver and a higher proportion of gastrointestinal neoplasms, particularly those of the stomach and esophagus. The highest levels of alcoholism and associated intestinal tumors occur in foreign, notably Spanish, agricultural workers who are paid in part with 2-3 liters of wine daily. (10 refs.)

77-5352 **Gastric Carcinoma in Man in Erfurt County (East Germany) During 1960-1969. Analysis of the Major Characteristics.** (Ger) Pothe, H. (Chirurgische Klinik der Medizinischen Akademie, Nordhauser Strasse 74, DDR-50 Erfurt, E. Germany); Usbeck, W.; Voigtsberger, P.; Bohm, W.; Schumann, E.; Kleinschmidt, H.; Goldhammer, D.; Knappe, G. *Dtsch Gesundheitswes* 32(18): 836-839; 1977.

According to a survery of the years 1960-1969, the Erfurt district had a relatively lower incidence of stomach cancer in men (45/100,000 men) than the rest of East Germany (58/100,000 men). Overall, 2,575 new cases of stomach cancer in men were diagnosed in Erfurt: 189 Stage I, 561 Stage II, 879 Stage III, and 889 Stage IV cancer; no data were available for 57 patients. The malignancy was diagnosed clinically in 14.3% of the patients, macroscopically during surgery in 12.1%, histologically in 40.5%, roentgenologically in 27.3%, and at autopsy in 3.2%; the diagnosis was not known in 2.6%. Of the 2,575 patients, 1,616 were operated on, with a postoperative mortality of 31.1%. Of 1,838 cases reported during the first 7 yr, only 4.7% survived 5 yr; however, 18.3% of 372 with partial resections survived 5 yr. (11 refs.)

77-5353 **Mortality due to Cancer of the Stomach, Colon and Rectum, and Food Consumption in Austria During the Period 1953-1974.** (Ger) Vutuc, C. (Hygiene-Institut der Universitat Wien, Kinderspitalgasse 15, A-1095 Vienna, Austria); Kunze, M.; Gredler, B. *Wien Med Wochenschr* 127(5): 170-172; 1977.

study was made of mortality due to cancer of the stomach, olon, and rectum and of food consumption in Austria from 953-1974. The results showed that stomach cancer was inersely correlated with colorectal cancer. Death from stomch cancer decreased significantly from 1960 on (by 33% for nen, 19% for women). However, the mortality due to coloectal cancer increased significantly (by 54% and 23% in nen, 67% and 48% in women, respectively). During this eriod the av calorie intake increased from 2,726 calories in 953 to 3,058 calories in 1974. The decrease in stomach caner but increase in colorectal cancer correlated significantly vith an increase in the consumption of fat, animal protein, ggs, beer, and wine and a decrease in the consumption of otatoes, flour, and milk. The incidence of rectal cancer howed a significant correlation with the increase in sugar onsumption. (21 refs.)

7-5354 **Changing Distribution of Primary Cancers in the Large Bowel.** (Eng) Rhodes, J. B. (Dept. Medicine, Univ. Kansas Medical Center, Rainbow Blvd. at 9th, Kansas City, KS 66103); Holmes, F. F.; Clark, G. M. *AMA* 238(15): 1641-1643; 1977.

n analysis of the changing distribution of the origin site of ,990 colorectal cancers observed at a large midwestern hosital from 1946 through 1975 showed a statistically signifiant trend of a decreasing percentage of distal (rectum) and n increasing percentage of proximal (cecum) large-bowel esions. Mortality data for 11,635 colorectal cancers in Kanas for this period confirm this trend. The respective decrease nd increase may well be the result of more than one factor perating concurrently. Digital examination of the rectum nd sigmoidoscopy are less likely to diagnose large-bowel ancer than they did 30 yr ago. Stool screening for occult lood, barium enema roentgenographic examination, and olonoscopy are now more important diagnostic tools. (8 efs.)

7-5355 **Changes in Site Distribution of Colorectal Carcinoma in Connecticut, 1940-1973.** (Eng.) Snyder, D. N. (Connecticut Cancer Epidemiology Unit, 30 College St., New Haven, CT 06510); Heston, J. F.; Meigs, J. W.; lannery, J. T. *Am J Dig Dis* 22(9): 791-797; 1977.

nalysis of the 40,771 cases reported in Connecticut over the ast 34 yr revealed that the distribution of primary colorectal ancer has changed proportion among subsites in the bowel. The rise in both proportion of cases and incidence rate of scending colon cancer is particularly significant and does ot appear to be due to misclassifications. Increases in upper olon cancers were greatest in people over 65 yr of age. (12 efs.)

77-5356 **An Epidemiological Study of Stomach Cancer.** (Rus.) Gaidei, V. V. (Dept. Social Hygiene and Health Protection Organization, Vinnitsa Medical Inst., Vinnitsa, USSR) *Vrach Delo* (4): 143-147; 1977.

The role of environmental factors in morbidity due to stomach cancer is discussed, and the importance of an epidemiological approach for the prevention and treatment of this cancer is emphasized. All patients with stomach cancer should complete a special questionnaire consisting of five main sections: (1) data on the patient's occupation; (2) data on living conditions (ie, income, family size); (3) data on hereditary predisposition to neoplasia; and (5) data on the clinical features of stomach cancer (duration of disease, treatment, concomitant diseases). Statistical analysis of the data might help to determine other factors and increased risk groups. (no refs.)

77-5357 **Epidemiological Features of Canine Renal Neoplasms.** (Eng.) Hayes, H. M. (Environmental Epidemiology Branch, NCI, NIH, Bethesda, MD 20014); Fraumeni, J. F. *Cancer Res* 37(8/Part 1): 2553-2556; 1977.

A retrospective study of 73 cases of canine primary renal neoplasms indicated no breed predisposition, but an excess risk was noted in males in middle age. Because of the similarity of this neoplasm to renal carcinoma in humans, the dog may be a suitable model for research. (50 refs.)

77-5358 **Incidence Patterns of Spontaneous Tumors in BN/Bi Rats.** (Eng.) Burek, J. D. (Inst. Experimental Gerontology TNO, 151 Lange Kleiweg, Rijswijk ZH, Netherlands); Hollander, C. F. *J Natl Cancer Inst* 58(1): 99-105; 1977.

The occurrence of tumors in 236 female and 74 male BN/Bi rats that were allowed to live out their normal life spans is described. For most neoplasms, the risk of a rat dying with a specific tumor increased with age. Some tumors, however, had a peak incidence: therefore, animals surviving these periods were at less risk than their younger cohorts. These tumors included mammary gland fibroadenomas and ureter carcinomas in females and bladder and ureter carcinomas in males. The number dying with metastatic cancers was greatest in females > 30 mo of age. Unexpectedly, males had a peak risk period at 25-30 mo, so that males that died in older age groups had less risk of dying with a metastatic tumor. Lesions were often multiple, even in rats dying at a young age. The percentage of dead rats with multiple tumors did not increase significantly with age. Some animals in every age group died without a tumor, and the percentage without neoplasms did not decrease, even in the older age groups. (17 refs.)

77-5359 **Bovine Leukemia Virus Specific Antibodies Among French Cattle. I. Comparison of Complement Fixation and Hematological Tests.** (Eng.) Levy, D. (Laboratoire d'Immunologie et de Virologie des Tumeurs, INSERM U 152, Hopital Cochin, 75014, Paris, France); Deshayes, L.; Guillemain, B.; Parodi, A. L. *Int J Cancer* 19(6): 822-827; 1977.

Complement fixation and hematological studies were performed on 517 French cows in different geographical regions to test for bovine leukemia virus specific antibodies. The serologic test revealed approx twice as many positive animals as the hematologic test did. In herds that had had several cases of leukemia, animals were more frequently positive than in leukemia-free herds in high risk (exposed) regions. Ther were no positive animals in leukemia-free and apparentl unexposed herds. (19 refs.)

See also:
* (Rev.): 77-4801, 77-4803, 77-4805, 77-4809, 77-481 77-4811, 77-4816, 77-4817, 77-4818, 77-4823, 77-482 77-4828, 77-4832, 77-4834, 77-4835, 77-4836, 77-485 77-4869, 77-4870, 77-4871, 77-4872, 77-4873, 77-487 77-4875, 77-4876, 77-4877.
* (Chem.): 77-4926, 77-4950, 77-4988, 77-4996, 77-500 77-5010.
* (Phys.): 77-5025, 77-5027, 77-5028, 77-5029, 77-503 77-5033, 77-5034, 77-5053.
* (Immun.): 77-5194, 77-5211.
* (Path.): 77-5307, 77-5316.

77-5360 **Nucleic Acid Content and Nuclear Chromatin Structure of Human Bladder Cell Culture Lines as Studied by Flow Cytofluorometry.** (Eng.) Melamed, M. R. (Cytology Service, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021); Darzynkiewicz, Z.; Traganos, F.; Sharpless, T. K. *Cancer Res* 37(4): 1227-1231; 1977.

Studies of two human bladder cell lines, HCV-29 and T-24 revealed differences in cytological morphology, especially nuclear chromatin structure and staining, consistent with their respective origins from benign and malignant bladder epithelium. The two cell lines showed different DNA "melting curves". The RNA/DNA ratio for HCV-29 was over twice as high as for T-24. (28 refs.)

77-5361 **Early Effects of Phytohemagglutinin on Induction of DNA Polymerase, Thymidine Kinase, Deoxyribonucleoside Triphosphate Pools and DNA Synthesis in Human Lymphocytes.** (Eng.) Tyrsted, G. (Dept. Biochemistry C, Univ. Copenhagen, Panum Inst., Blegdamsvej 3, 2200 Copenhagen N, Denmark); Munch-Petersen, B. *Nucleic Acids Res* 4(8): 2713-2723; 1977.

The temporal sequence of the induction of DNA polymerase, thymidine kinase, deoxyribonucleoside triphosphate pools, and DNA synthesis in human lymphocytes by phytohemagglutinin (PHA) was studied. DNA polymerase and thymidine kinase activity increased simultaneously after 15 hr of incubation with PHA. Thymine triphosphate (TTP) and deoxycytidine triphosphate (dCTP) pools expanded after 17 hr, and deoxyadenosine triphosphate and deoxyguanidine triphosphate (dGTP) pools enlarged after 21 hr. The incorporation of labeled dGTP into DNA increased simultaneously with the expansion of the TTP and dCTP pools. Incubation with PHA plus actinomycin prevented the induction of thymidine kinase and DNA polymerase activity, which suggests that the induction sequence results from effects at the levels of transcription and translation. (29 refs.)

77-5362 **Foreign DNA of Bacterial Plasmid Origin Is Transcribed in Crown Gall Tumours.** (Eng.) Drummond, M. H. (Dept. Microbiology and Immunology, Univ. Washington, Seattle, WA 98195); Gordon, M. P.; Nester, E. W.; Chilton, M. D. *Nature* 269(5628): 535-536; 1977.

Investigations of RNA transcription revealed transcripts of foreign genetic information in *Agrobacterium tumefaciens*-induced crown gall tumor cells. The study also indicated that labeled tumor RNA can be used to identify DNA fragments within the restriction endonuclease digest that contain oncogenic plasmid DNA base sequences transferred to the tumor. (13 refs.)

77-5363 **Variability of DNA Content of Murine Fibrosarcoma Cells.** (Eng.) Suzuki, N. (Section Experimental Radiotherapy, Univ. Texas System Cancer Center, M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX 77030); Withers, H. R.; Lee, L. Y. *Nature* 269(5628): 531-532; 1977.

Several clones from a methylcholanthrene-induced mouse fibrosarcoma were investigated for their DNA content by addition of spleen cell suspensions from normal C3Hf/Bu mice. Relative DNA content ranged from 1.49 to 3.07 with the original fibrosarcoma at 1.45. These results are consistent with the findings of aneuploidy and hyperploidy in malignant cells and imply that all the cells were able to vary DNA content. (16 refs.)

77-5364 **Reverse Transcription of Thyroglobulin 33-S mRNA.** (Eng) Dinsart, C. (Institut de Recherche Interdisciplinaire en Biologie Humaine et Nucleaire, Faculte de Medecine de l'U.L.B., Rue Evers 2, B-1000 Brussels, Belgium); Van Voorthuizen, F.; Vassart, G. *Eur J Biochem* 78(1): 175-181; 1977.

Bovine thyroglobulin 33S messenger RNA (mRNA) was used as a template for the synthesis of a complementary DNA (cDNA) using RNA-directed DNA polymerase from avian myeloblastosis virus. The reaction was not very efficient (thyroglobulin mRNA was about 10 times less efficient than Hb mRNA as a template for cDNA synthesis), and the size of the cDNA did not exceed 10S. However, a copy of high specific radioactivity (10^7 cpm/μg) could be obtained that hybridized specifically back to its template with an $r_0t1/2$ value (the product of RNA concentration and time, giving half-max hybridization of the cDNA with RNA in excess) five times higher than that observed in hybridizations between Hb mRNA and Hb cDNA. This indicates that thyroglobulin mRNA does not contain extensive internal repetitive sequences. Quantification of thyroglobulin mRNA sequences among various RNA preparations from beef thyroid was performed using cDNA/RNA hybridizations in an excess of RNA. The results confirmed that thyroglobulin mRNA represents the large majority of mRNA in membrane-bound polysomes and indicated that free polysomes do not contain a reservoir of inactive thyroglobulin mRNA. The cDNA transcribed from mRNA of bovine origin hybridized efficiently with thyroid RNA from goats, dogs, and humans. The species could be classified in the following order of decreasing sequence homology on the basis of the melting profile of the different hybrids: beef, goat, dog, and human. It is concluded that thyroglobulin cDNA, although representative only of part of the thyroglobulin sequence, provides a promising approach to the study of gene expression in the mammal thyroid. (39 refs.)

77-5365 **Effect of Tryptophan and Nicotinamide Loads on Urinary Excretion of RNA Metabolites by Bladder Cancer Patients: Brief Communication.** (Eng.) Nielsen, H. R. (Dept. Clinical Chemistry, Sundby Hosp., Italiensvej 1, DK-2300 Copenhagen S, Denmark); Wolf, H.; Brown, R. R. *J Natl Cancer Inst* 59(3): 855-858; 1977.

The effect of L-tryptophan and nicotinamide on the urinary excretion of the RNA metabolites β-aminoisobutyric acid, 7-methylguanine, pseudouridine, and urate was studied in 12 male bladder cancer patients. Upon administration of tryptophan (2 g po) the excretion of pseudouridine and 7-methylguanine decreased from 0.25-1.06 millimoles(mmol)/24 hr and 27-80 μmol/24 hr, respectively, to 0.15-0.64 mmol and 10-55 μmol. Urate excretion dropped from 2.18-4.20 to 2.03-3.50 mmol/24 hr, but β-aminoisobutyric acid excretion was relatively unchanged. Similar results followed the administration of nicotinamide (50 mg, po, qid). These findings suggest a possible common mode of action for tryptophan and nicotinamide. No definite mechanism for the observed decline in RNA turnover was determined. (20 refs.)

77-5366 **Effect of MOPC-315 Tumor DNA on Tumor** Development in Balb/c Mouse (Meeting Abstract). (Eng.) Naseem, S. M. (Channing Lab., Harvard Medical Sch., 774- Albany St., Boston, MA 02118) *Proc Am Assoc Cancer Res* 18: 187; 1977. (no refs.)

77-5367 **Demonstration of N-Acetylgalactosaminyl Transferase Activity During the Course of YC8 Murine Lymphoma.** (Fre.) Raimond-Pironneau, F. (Institut d'Immuno-Biologie de l'I.N.S.E.R.M., Hopital Broussais, 96, rue Didot, 75674 Paris Cedex 14, France) Achy-Sachot, N.; Turpin, M.; Morel, E. *C R Acad Sci D (Paris)* 284(16): 1597-1600; 1977.

N-Acetylgalactosaminyltransferase has been implicated in the synthesis of glycolipids of cell membranes, and several studies have attempted to relate cell glycosyltransferase activity to malignant cell transformation or tumor growth. It is postulated that the enzyme is present in the biological fluids circulating around the tumor. The serum, peritoneal fluid, and urine of male BALB/c mice bearing the YC8 lymphoma were assayed for N-acetylgalactosaminyltransferase activity. The mice were inoculated ip with 0.5 ml of a cell suspension of 1 x 10^6/ml YC8 ascites cells, and biological fluids were assayed for enzyme activity on days 3, 7, 9, and 13 after injection. Enzyme activity was enhanced 1-30 times in the peritoneal fluid and 1-10 times in the sera, but no enzyme activity was detected in the urine. The highest enzyme activity was obtained when 0.1 M Tris-HCl was used in the presence of 0.2 M Mn^{++}. The results suggest that not only are increased amounts of the enzyme synthesized during tumor growth, but synthesis of molecules that are endogenous acceptors of the enzyme is enhanced. (8 refs.)

77-5368 **Study of Lysosomal Neuraminidase, β-Galactosidase, and β-Acetylglucosaminidase in Regenerating Rat Liver.** (Rus.) Valiakina, T. I. (M. M. Shemiakin Inst. Bioorganic Chemistry, Acad. Sciences USSR, Moscow, USSR); Gabrielian, N. D.; Komaleva, R. L.; Khorlin, A. Ia. *Biokhimiia* 42(3): 513-518; 1977.

The distribution and activity of neuraminidase (NA), β-galactosidase (BG), and β-N-acetylglucosaminidase (AGA) were studied in the regenerating livers of random-bred albino rats subjected to partial hepatectomy. The enzymes were located predominantly in the lysosome fraction. However, 24 hr after hepatectomy, lysosomal NA activity was significantly elevated (8.4 units, compared to 3.0 units in controls), but that of BG and AGA was markedly decreased (0.06 and 0.47 unit, respectively, compared to 0.3 and 33.1 units in controls). (17 refs.)

77-5369 **Increase in Serum and Tissue Glycosyltransferases and Glycosidases in Tumor-bearing Rats.** (Eng.) Ip, C. (Dept. Breast Surgery, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY 14263); Dao, T. L. *Cancer Res* 37(9): 3442-3447; 1977.

Two glycosyltransferases (sialyltransferase, ST, and galactosyltransferase GT) and two glycosidases (sialidase SD and β-galactosidase β-GD) were examined in the serum, liver, and tumor of Sprague-Dawley rats with either 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary tumors (that grow slowly) or transplantable Walker carcinomas 256 (that grow rapidly) to determine whether enzymes in different tissues involved in glycoprotein metabolism can indicate tumor proliferation. In rats bearing the DMBA-induced mammary tumors, there was no significant increase in serum ST activity until the tumor load was 10-20 g. This was accompanied by a 60% increase in the liver ST. No change was detected in the levels of serum and liver GT. The increase in serum and liver ST and GT in rats bearing the Walker carcinomas paralleled the wt of the growing tumor mass. The magnitude of increase in both enzymes was higher than that in rats carrying a similar load of DMBA-induced tumor. β-GD and SD activities were elevated only in the serum of rats carrying the Walker carcinomas, but there was no relationship between increment of enzyme levels and tumor mass. These results suggest that the level of the enzyme activities may be a function of tumor growth rate and that tumor growth can lead to other physiological events that are remote from the primary tumor sites; ie the elevation of certain host liver glycosyltransferases. (29 refs.)

77-5370 **Binding and Internalization of Thrombin by Normal and Transformed Chick Cells.** (Eng.) Zetter, B. R. (Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA 02139) Chen, L. B.; Buchanan, J. M. *Proc Natl Acad Sci USA* 74(2): 596-600; 1977.

Thrombin stimulated cell proliferation in cultures of normal chick embryo fibroblasts (CEF) but not in cells transformed with Rous sarcoma virus (RSV). Analysis of medium conditioned by RSV-transformed cultures demonstrated that these cells did not secrete molecules that can inhibit or inactivate thrombin. The interaction of thrombin with CEF was investigated with enzymatically active ^{125}I-thrombin. The total amount of cell-associated ^{125}I-thrombin was three times greater in normal cells than in transformed cells. In both, $>50\%$ of the total cell-associated ^{125}I-thrombin was found as a component that was not dissociated from the cells by trypsin treatment, an observation suggesting that a significant portion was not on the cell surface. The amount of the trypsin-insensitive fraction increased with time up to 12 hr, but the trypsin-sensitive fraction was saturated after 1-4 hr. Autoradiography of thin sections of ^{125}I-thrombin-treated cells observed by electron microscopy revealed that after 10 hr incubation, $>70\%$ of the label is localized in the cytoplasm of both normal and transformed cells. Autoradiograms of sodium dodecyl sulfate-polyacrylamide slab gels demonstrated that 40% of the intracellular label is the size of native thrombin, with the remainder in two large fragments of 22,000 and 19,500 daltons. (14 refs.)

77-5371 **Distribution of Cell Surface LETS Protein in Co-cultures of Normal and Transformed Cells.** (Eng) Chen, L. B. (Cold Spring Harbor Lab., Cold Spring Harbor, NY 11724); Moser, F. G.; Chen, A. B.; Mosesson, M. W. *Exp Cell Res* 108(2): 375-383; 1977.

Immunofluorescence was used to investigate the control of expression of surface large external transformation sensitive (LETS) protein by co-cultivating CCL47 rat sarcoma and CCL49 Syrian hamster melanoma cells with chicken embryo fibroblasts. Side-by-side co-cultivation of both malignant lines with the fibroblasts and growth of the malignant lines on top of and under the normal cells did not influence the distribution of the LETS protein. Furthermore, no reduction in fibrinolytic activity of transformed cells was observed after co-cultivation of transformed cells with untransformed cells at different ratios. The addition of up to 100 μg/ml of α_2-macroglobulin or up to 50 μg/ml of transglutaminase to the cultures did not restore either normal morphology or LETS distribution on transformed cells, nor did protease inhibitors restore LETS distribution. It is suggested that unknown mechanisms govern the distribution of LETS protein on the surface of cultured cells. (19 refs.)

77-5372 **The Major Surface Protein of Epithelial Cells from Newborn and Adult Rat Livers in Primary Cultures.** (Eng.) Marceau, N. (Laboratoire de Biophysique Medicale CHUL, Ste-Foy, Quebec, Canada G1V 4G2); Robert, A.; Mailhot, D. *Biochem Biophys Res Commun* 75(4): 1092-1097; 1977.

A major protein (mol wt 80,000 daltons) was found on the surface of epithelial cells from newborn and adult rat liver by lactoperoxidase-catalyzed iodination. The significance of this epithelial protein in cell adhesion, antigenicity and malignant transformation is discussed. (19 refs.)

77-5373 **Nuclear Protein Phosphokinases in Normal and Neoplastic Tissues.** (Eng.) Thomson, J. A. (Dept. Biochemistry, J. Hillis Miller Health Center, Univ. Florida, Gainesville, FL 32610); Chiu, J. F.; Sakuma, K.; Hnilica, L. S. *Cancer Res* 37(9): 3266-3273; 1977.

Protein phosphokinases were isolated from the nuclei of normal and fetal rat liver and neoplastic tissues and chromatographed on phosphocellulose columns that resolved the normal and fetal liver kinases into five reproducible fractions. All five fractions differed in their $Mg^{2}+$ and $Mn^{2}+$ optimal concentrations as well as in their substrate specificities. They also phosphorylated different species of nuclear nonhistone proteins, as judged by polyacrylamide gel electrophoresis. Hepatic proliferation was accompanied by quantitative changes in the kinase activity profiles using endogenous phosphoprotein as a natural substrate. An additional phosphoprotein kinase activity stimulated by $Mn^{2}+$ was found in the nuclei of malignant cells (Walker tumor, Novikoff ascites hepatoma, and Ehrlich ascites tumor). This tumor-specific kinase could not be detected either in the tumor cytoplasm or in fetal or regenerating liver nuclei. Mn^{2+}-dependent phosphoprotein kinase from Novikoff hepatoma phosphorylated only one major protein band detectable by polyacrylamide gel electrophoresis. This substrate could not be detected in the chromatin of normal tissues. These results indicate that neoplastic growth may be associated with highly specific alterations of the transcriptional control mechanism. (31 refs.)

77-5374 **Decreased Incorporation of Phosphate and Amino Acids into Low-Solubility, Nuclear Proteins in Rapidly Growing Hepatomas.** (Eng.) Lea, M. A. (Dept. Biochemistry, New Jersey Medical Sch., Newark, NJ 07103); Koch, M. R. *Int J. Biochem* 8(8): 565-572; 1977.

An investigation of nonhistone chromosomal proteins revealed that the incorporation of ^{32}P-phosphate and ^{3}H-labeled amino acids was reduced in a low-solubility fraction of nuclear proteins from neoplastic rat liver, compared with normal liver. The phosphate content of four nuclear protein fractions (0.14 M NaCl extract, 0.35 M NaCl extract, histones, residual nuclear proteins) from the slow-growing hepatoma 7787 did not differ significantly from that of the host liver. However, in the more rapidly growing hepatomas 7777 and $9618A_2$, the phosphate contents of the NaCl extracts and histones were greater than those in host livers, but the phosphate content of the residual nuclear proteins was decreased to 45% ($p < 0.001$) and 55% ($p < 0.001$) of the respective host liver values. ^{32}P-phosphate incorporation into the residual nuclear protein fraction of regenerating liver was similar to that of the host liver. Studies on the incorporation of ^{3}H-labeled amino acids revealed low rates for the low-solubility nonhistone nuclear protein fraction in the rapidly growing hepatomas $9618A_2$ and 7777 relative to the slowly growing hepatoma 20 and regenerating, control, and host livers. The data suggest that a decreased metabolism of this residual nuclear protein fraction is not an inherent feature of either neoplastic or rapid growth but may be present with a combination of these factors. (30 refs.)

77-5375 **Free Carboxylate Groups Required for Transport of Neutral Amino Acids by the Ehrlich Ascites-tumor Cell.** (Eng.) Garcia-Sancho, J. (Dept. Biological Chemistry, Univ. Michigan, Ann Arbor, MI 48109); Sanchez, A.; Christensen, H. N. *Biochim Biophys Acta* 465(2): 426-428; 1977.

Experimental results are presented which strongly suggest that the free alpha-carboxyl group is needed in the carboxylate form for transport of the amino acid molecule into the Ehrlich ascites tumor cell via Systems A or L. (6 refs.)

77-5376 **Comparison of Octopine, Histopine, Lysopine, and Octopinic Acid Synthesizing Activities in Sunflower Crown Gall Tissues.** (Eng.) Hack, E. (Dept. Plant Pathology, Agricultural Res. Service, US Dept. Agriculture, Univ. Wisconsin, Madison, WI 63706); Kemp, J. D. *Biochem Biophys Res Commun* 78(2): 785-791; 1977.

The in vitro synthesis of octopine, histopine, lysopine and octopinic acid by tissue extracts of sunflower crown gall tumors induced by *Agrobacterium tumefaciens* strain B_6 was analyzed. NADPH or NADH, pyruvate and the appropriate amino acids were required. It is suggested that the same enzyme may be involved in the synthesis of all four amino acids. (16 refs.)

77-5377 **A Useful Synthesis of Nopaline, a Crown Gall Tumor Metabolite.** (Eng.) Jensen, R. E. (Dept. Chemistry, Univ. Washington, Seattle, WA 98195); Zdybak, W. T.; Yasuda, K.; Chilton, W. S. *Biochem Biophys Res Commun* 75(4): 1066-1070; 1977.

A method for synthesizing nopaline is described. Reduction of L-arginine and α-ketoglutaric acid with sodium cyanoborohydride gave an 80% yield of the diastereoisomers nopaline and isonopaline. (15 refs.)

77-5378 **The Specificity of Glutamine Metabolism in Precancerous Diseases and in Human Gastric Carcinoma.** (Rus) Berezov, T. T. (Chair of Biochemistry, Faculty of Medicine of P. Lumumba Univ., Moscow, USSR); Aptekar', L. S.; Zinevich, A. K. *Vopr Med Khim* 23(4): 555-558; 1977.

Free glutamine content, and the activity of glutamine synthetase and glutamine transaminase were studied in the ulcer areas in polyps and in malignant neoplasms, and in the unaffected mucous membrane and whole blood of patients with chronic atrophic gastritis, ulcer disease, polyposis and gastric carcinoma, as well as of healthy controls. Glutamine content was decreased in the blood of patients with gastric carcinoma and increased in the mucous membranes adjacent to the malignant tissue. Glutamine transaminase activity was found in precancerous lesions; this activity was absent in normal gastric mucosa. (14 refs.)

77-5379 **Neutral Amino Acid Transport in Surface Membrane Vesicles Isolated from Mouse Fibroblasts: Intrinsic and Extrinsic Models of Regulation.** (Eng) Lever, J. E. (Salk Inst. Biological Studies, P. O. Box 1809, La Jolla, CA 92112). *J Supramol Struct* 6(1): 103-124; 1977.

An investigation was made of the coupling between electrochemical Na+ gradients, membrane potential, and accumulation of neutral amino acids via functional components of cellular uptake systems using Swiss and BALB/c 3T3 mouse fibroblasts transformed by simian virus 40, BALB/c tertiary mouse embryo cells, and Swiss 3T3 fibroblasts. When Na+ was preequilibrated across the membrane to abolish active accumulation, countertransport was demonstrated. The competitive interactions among neutral amino acids for transport into vesicles were similar to those previously reported for uptake in Ehrlich ascites cells, and they indicated that the A and L systems and a glycine system were functional in the vesicles. When an Na+ gradient (external > internal) was generated across the membrane, the initial rate and steady state of alanine and glycine uptake were markedly increased. The pH profiles and Km values for alanine and 2-aminoisobutyric acid transport into the vesicles were those expected for the corresponding cellular uptake system. With the A and the glycine systems, the initial rate and quasi-steady state of accumulation were stimulated as a function of increasing Na+ concentrations, indicating that Na+ is part of the driving force of transport. Further studies indicated the presence of an electrogenic mechanism in which amino acid translocation is coupled to the Na+ gradient by formation of a positively charged complex of Na+, amino acid, and membrane component. Vesicles from transformed cells exhibited an increased Vmax for Na+-stimulated 2-aminoisobutyric acid transport and an increased capactiy for steady-state accumulation of amino acids. Possible regulatory interactions for these systems are discussed. (55 refs.)

77-5380 **Growing Human Sarcomas in Culture.** (Eng) Sethi, J. (Sloan-Kettering Inst. Cancer Res., 425 E. 68th St., New York, NY 10021); Hirshaut, Y.; Hajdu, S. I.; Clements, L. G. *Cancer* 40(2):744-755; 1977.

Efforts to establish human soft tissue and bone sarcomas in long-term cultures are described, and characteristics of the cell lines established are reported. Of 49 attempts, 22 were successful, yielding cells that proliferated in vitro for ≥ 6 mo. Infrequent medium changes, maintenance of pH in the physiologic range, and avoidance of early trypsinization were important for survival and initial growth of the explanted cells. All 12 of the tumor lines studied cytologically showed distinct characteristics of malignancy and sufficient cytologic criteria to classify these cell cultures as derived from mesenchymal rather than epithelial tissues. (21 refs.)

77-5381 **Polymer Aggregation and Cell Adhesion.** (Eng.) Maroudas, N. G. (71 Park Ave. North, London, NW10 1LE, England). *Prog Clin Biol Res* 17: 511-520; 1977.

Polymer aggregation and baby hamster kidney cell adhesion were studied on gels of differing molecular aggregation. The cellular adhesiveness of polymers increased with concentration; the size of the individual aggregates approached that of filopodia. It is suggested that cell adhesion to neutral hydrogels occurs by a colligative process involving an equilibrium between polymer exclusion and adsorption at dense, localized aggregates. (24 refs.)

77-5382 **Correlation of Cellular Aggregation of Transformed Cells with Their Growth in Soft Agar and Tumorigenic Potential.** (Eng) Putman, D. L. (Microbiological Associates, Inc., Bethesda, MD 20016); Park, D. K.; Rhim, J. S.; Steuer, A. F.; Ting, R. C. *Proc Soc Exp Biol Med* 155(4): 487-494; 1977.

A new aggregation assay that can be used to monitor the tumorigenic potential of spontaneous-, virus-, or chemical-transformed cells of various animal species is presented. Formation of cellular aggregates by transformed rat, mouse, hamster, and human cells was compared with aggregate formation by untransformed control cells. The viability and proliferation of aggregated cells and their growth in soft agar correlated well with tumorigenic potential, regardless of the method of transformation. It is concluded that this assay could provide an easy and accurate means of evaluating in vitro cell transformation. (21 refs.)

77-5383 **The Kinetics of Contact Inhibition in Mammalian Cells.** (Eng.) Schmialek, P. (Zentralinstitut fur Biochemie und Biophysik der Freien Universitat Berlin, Arnimallee 22, D 1000 Berlin 33, W. Germany); Geyer, A.; Miosga, V.; Nundel, M.; Zapf, B. *Cell Tissue Kinet* 10(2): 195-202; 1977.

[^{3}H]thymidine labeled embryonic Chinese hamster cells were cocultured with various concentrations of isotope-free cells. After contact inhibition concentration was reached, the cells continued to grow for one more generation. In the next 24 hr, the cell population fell back to the original level and remained there. (24 refs.)

77-5384 **Loss of Growth Control and Differentiation in the fu-1 Variant of the L_8 Line of Rat Myoblasts.** (Eng) Kaufman, S. J. (Dept. Microbiology, Univ. Illinois, Urbana, IL 61801); Parks, C. M. *Proc Natl Acad Sci USA* 74(9): 3888-3892; 1977.

The L_8 line of rat myoblasts and the non-fusing variant, fu-1, were investigated. A comparison of the growth rates yielded a doubling time of 19.1 hr for L_8 cells and 14.8 hr for fu-1 cells; the fu-1 cells also grew to 10-fold higher densities than L_8. This was partially due to overgrowth of fu-1 cells and the larger area of cells of the parent line. Serum requirement studies revealed that the max density of fu-1 cells in 1% serum was more than 25-fold greater than that of L_8 cells; the two lines could also be distinguished by their different rates of detachment. The growth characteristics in soft agar and the 2-deoxyglucose uptake of fu-1 cells suggested transformation. fu-1 Cells injected sc in nu/nu mice resulted in tumor formation; this was not observed with L_8 cells. Creatin kinase and myosin were not present in increased quantities in fu-1 cells, while these were present following fusion in the parent line. These findings suggest that loss of the ability to differentiate normally is associated with the loss of normal control of cell division of myoblasts grown in vivo and in vitro. (43 refs.)

77-5385 **Density-dependent Inhibition of Fibroblast Growth Is Overcome by Pure Mitogenic Factors.** (Eng) Mierzejewski, K. (Imperial Cancer Res. Fund Lab., Lincoln's Inn Fields, London, England); Rozengurt, E. *Nature* 269(5624): 155-156; 1977.

Chemically defined molecules, rather than whole serum, were added to sparse or crowded cultures of 3T6 cells arrested in G_0/G_1 to determine the effect on growth inhibition. When epidermal growth factor (EGF) and insulin were added at low concentrations to low density cultures (0.5 x 10^4 cells/cm^2), DNA synthesis was stimulated, suggesting that pure peptides do not act by diminishing inhibitory cell-cell contacts. High concentrations of these factors were also able to stimulate DNA synthesis in dense cultures. This effect was observed when the incubation time was either 24 or 48 hr. Therefore, high factor levels can overcome density-dependent inhibition of growth. It is believed that the action of insulin is related to its hormonal effect for the following reasons: the B chain of the hormone was ineffective in stimulation; B chain added to low concentrations of insulin and EGF did not overcome density dependent inhibition in crowded cultures; and inhibitors of the proteolytic activity of insulin had no effect on growth enhancement by insulin and EGF at high concentrations. (10 refs.)

77-5386 **Stimulation of Corneal Endothelial Cell Proliferation In Vitro by Fibroblast and Epidermal Growth Factors.** (Eng) Gospodarowicz, D. (Cancer Res. Inst., Univ. California, Medical Center, San Francisco, CA 97143); Mescher, A. L.; Birdwell, C. R. *Exp Eye Res* 25(1): 75-89; 1977.

A bovine corneal endothelial cell (CEC) culture was developed to study factors controlling corneal endothelial proliferation. The proliferation of CEC in culture was greatly stimulated by both fibroblast growth factor (FGF) and epidermal growth factor (EGF). Both FGF and EFG are mitogenic for CEC; FGF or EFG reduced the cell doubling time to 20-24 hr from 48 hr for cells maintained at low density in 5% plasma. The final cell density reached in the presence of either growth factor was 10 times that of cells maintained in 5% plasma alone. CEC in 1% serum with FGF reached a final density identical to that in 10% serum alone; addition of FGF to 10% serum resulted in a final density that was three times that of 10% serum alone. The half-max response for the stimulation of proliferation was at 6 x 10^{-10} M for FGF and 1.5 x 10^{-10} M for EFG Stimulating of DNA synthesis in resting cultures occurred with 7 x 10^{-13} to 7 x 10^{-9} M FGF and 1.5 x 10^{-15} to 1.5 x 10^{-13} M EFG. Inclusion of FGF in the medium permitted cloning of CED from cultures seeded at low density (0.6 cell/cm^2). (28 refs.)

77-5387 **Control of a Cell Surface Major Glycoprotein by Epidermal Growth Factor.** (Eng.) Chen, L. B. (Cold Spring Harbor Lab., Cold Spring Harbor, NY 11724); Gudor, R. C.; Sun, T. T.; Chen, A. B.; Mosesson, M. W. *Science* 197(4305): 776-778; 1977.

Confluent 3T3 mouse cells growing in culture supplemented with 10% calf serum had massive fibrillar networks of large external transformation sensitive (LETS) protein. However, when the medium was changed to 0.7% serum, most of the LETS protein disappeared. Among 13 hormones and growth factors tested for their influence on the expression of LETS protein, only epidermal growth factor (EGF) had an effect. EGF could induce the reappearance of the massive network of fine fibers of LETS protein in low-serum cultures of 3T3 cells. These results suggest that some of the differentiated functions of a given cell type are controlled by hormones. (23 refs.)

77-5388 **Effects of Cellophane Tape Stripping of Mouse Skin on Epidermal Growth Regulators (Chalones).** (Eng) Rohrbach, R. (Pathologisches Institut, Albertstrasse 19, D-7800 Freiburg im Breisgau, W. Germany); Iversen, O. H.; Riede, U. N.; Sandritter, W. *Beitr Pathol* 160(2): 175-186; 1977.

The effects of cellophane tape (Tesafilm) stripping on the chalones of 3-mo-old hairless hr/hr Oslo strain mice were investigated. Fresh pieces of Tesafilm were applied to the skin of the back of the animals and immediately torn off; this was repeated six times in the same area. Epidermal mitotic activity and DNA synthesis were investigated at different times. Histologic examination revealed that the horny layer and upper row of differentiated cells and, occasionally, the entire epidermis had been removed 6 to 12 hr after treatment. Hyperplasia was noted on day 1 or 2, it increased by day 4 or 5, and it subsided with return of normal thickness after 3 to 4 wk. There was a short block in mitosis and probably in DNA synthesis. This was followed by bimodal peaks of increased activity, with the two maxima of (labeling index) on days 2 and 6 and the two maxima of mitotic activity recurring on days 1-2 and 7. G_1 and G_2 chalones were present in an inverse proportion to alterations in DNA synthesis and mitosis with one exception: a depression of the mitotic rate and a low G_2 chalone concentration. G_1 reappeared more slowly than G_2, reaching its highest activity on days 9-10 compared with days 4-5 for G_2. It is concluded that stripping removes the differentiating cells and injures the basal cells, altering chalone content. The resultant increase in DNA synthesis and in mitosis lasts only until the number of cells is high enough to produce chalones again. (15 refs.)

77-5389 **Transition Metal Ions Induce Cell Growth in NRK Cells Synchronized in G_1 by Picolinic Acid.** (Eng.) Fernandez-Pol, J. A. (Nuclear Medicine Lab., Veterans Admin. Hosp., St. Louis, MO 63125) *Biochem Biophys Res Commun* 76(2): 413-419; 1977.

The effects of ions on cell growth and on the growth inhibition induced by picolinic acid were studied in normal rat kidney (NRK) cells. The G_1 arrest induced in NRK cells by picolinic acid was prevented by addition of Fe^{3+}, Zn^{2+}, or Co^{2+} to the tissue culture media. Ca^{2+}, Mg^{2+}, Mn^{2+}, Sr^{2+}, or Ba^{2+} were ineffective. Co^{2+} reversed the G_1 block, but cells began to divide asynchronously after 30 hr. Addition of Fe^{3+} or Zn^{2+} to G_1-arrested cells, however, stimulated synchronous growth, Fe^{2+} to G_1-arrested cells, however, stimulated synchronous growth, Fe^{3+} being effective at lower concentration than Zn^{2+}. Thymidine incorporation, mitotic index, and relative DNA content per cell verified that G_1-arrested cells proceeded through the cell cycle after addition of Fe^{3+} or Zn^{2+}. These results indicate that the G_1 arrest induced by picolinic acid in NRK cells may be primarily due to chelation of Zn^{2+} and/or Fe^{3+}. They support the concept that availability of Fe^{3+} and/or Zn^{2+} within the cell may play a central role in the coordinated control of events leading to the initiation of DNA synthesis in G_1-arrested cells. (12 refs.)

77-5390 **Uptake of Hyaluronate by Cultured Cells.** (Eng) Truppe, W. (Inst. Medical Chemistry, Univ. Graz, A-8010 Graz, Austria); Basner, R.; von Figura, K.; Kresse, H. *Biochem Biophys Res Commun* 78(2): 713-719; 1977.

The uptake of labeled hyaluronate by human skin fibroblasts, smooth muscle cells from the human thoracic aorta, synovial cells and rat hepatocytes was investigated. The data indicated that only synovial cells and rat hepatocytes were able to incorporate the radioactivity by adsorptive pinocytosis. Extracellular hyaluronate was associated with cellular membranes unable to perform specific endocytosis; this observation accorded with the fact that pericellular hyaluronate pools were a normal constituent of some of these cells. The amount of hyaluronate which could be internalized was dependent on extracellular concentration; uptake showed the expected saturation kinetics. Pincytosed hyaluronate was rapidly degraded. Adsorption of hyaluronate onto the cell surface was also saturable. Competition experiments between labeled hyaluronate and unlabeled hyaluronate oligosaccharides were performed. All oligosaccharides competed less efficiently than unlabeled hyaluronate with the hexa- and octasaccharides being the most efficacious competitors for uptake. However, the labeled oligosaccharides were not internalized by hepatocytes, probably because of incomplete binding to the receptor molecule(s). (9 refs.)

77-5391 **Different Extracellular Calcium Requirements for Proliferation of Nonneoplastic, Preneoplastic, and Neoplastic Mouse Cells.** (Eng.) Boynton, A. L. (Animal and Cell Physiology Group, Div. Biological Sciences, Natl. Res. Council Canada, Ottowa, Ontario, Canada K1A OR6); Whitfield, J. F.; Isaacs, R. J.; Tremblay, R. G. *Cancer Res* 37(8, part 1): 2657-2661; 1977.

The extracellular free (or ionic) calcium (EFC) requirements for DNA synthesis and proliferation were examined in nonneoplastic, preneoplastic, and neoplastic mouse cells. DNA synthesis and proliferation in freshly isolated, nontumorigenic C3H mouse skin cells (first passage) were lowest when the EFC level was reduced to 0.05-0.1 milliM. The EFC level in cultures of repeatedly passaged, preneoplastic C3H/10T1/2 and MCA-C3H/10T1/2 type I mouse fetal fibroblasts had to be reduced to 0.01 milliM or less before DNA synthesis and proliferation were minimal. This inhibition of DNA synthesis and cell multiplication was rapidly reversed by returning the calcium level to its normal value. The neoplastic, fibrosarcoma-forming, MCA-C3H/10T1/2 type III mouse fetal fibroblasts could synthesize DNA and multiply indefinitely, even in the presence of an extremely low concentration of EFC. Whether the loss of proliferation control by calcium is an essential part or merely a side effect of neoplastic transformation of cells of mesenchymal origin remains to be determined. Despite this uncertainty, it is probable that the EFC requirement for DNA synthesis and proliferation will prove to be an indicator of the tumorigenic potential of a cell. (27 refs.)

77-5392 **Roles of Proteins from Inner Face of Plasma Membranes in Susceptibility of $(Na^+ + K^+)$-stimulated Mg^{2+} Adenosinetriphosphatase to Ouabain.**

(Eng.) Zachowski, A. (Station de Recherches de Virologie et d'Immunologie, Institut National de la Recherche Agronomique, Route de Thiverval, 78850 Thiverval-Grignon, France); Lelievre, L.; Aubry, J.; Charlemagne, D.; Paraf, A. *Proc Natl Acad Sci USA* 74(2): 633-637; 1977.

Purified right-side-out (RSO) and inside-out (IO) plasma membrane vesicles of cells derived from a murine plasmacytoma (MOPC 173) released 35% of the total plasma membrane proteins after EDTA treatment. The treated vesicles exhibited the same total activity of (Na^+ + K^+)-stimulated Mg^{2+} ATPase as in their native state. The EDTA treatment increased the enzyme sensitivity to ouabain by 350-fold in IO vesicles, but had no effect in RSO vesicles. Thus, only proteins released from the IO vesicles led to a change in ouabain sensitivity of the (Na^+ + K^+)-stimulated Mg^{2+} ATPase. Moreover, only proteins released from IO vesicles, when added to treated IO vesicles with divalent cations, were able to restore the original resistance of the enzyme to ouabain; proteins released from RSO vesicles lacked this ability. The EDTA-treated proteins that can modify enzyme activity are, therefore, detached from the inner face of the plasma membrane and are distinct from the enzyme. Polyacrylamide gel electrophoresis indicated that these proteins are approx 30,000 daltons. (22 refs.)

77-5393 **Effect of Exogenous ATP on the Permeability Properties of Transformed Cultures of Mouse Cell Lines.** (Eng.) Rozengurt, E. (Imperial Cancer Res. Fund, Lincoln's Inn Fields, London, England); Heppel, L. A.; Friedberg, I. *J Biol Chem* 252(13): 4584-4590; 1977.

The effect of exogenous ATP on the membrane permeability for metabolites and ions present inside various cells is described. The cell lines used were Swiss mouse 3T3 and 3T6 (a line derived from 3T3 by spontaneous transformation) cells, mouse embryo fibroblasts, SV3T3 and PY3T3 cells (3T3 cells transformed by simian virus 40 and by polyoma virus, respectively) and human lung embryo fibroblasts. ATP changed the membrane permeability of the transformed cultured mouse cells extensively, leading to a depletion of intracellular pools labeled with ^{3}H-uridine, ^{3}H-adenosine, ^{86}Rb, or ^{3}H-2-deoxyglucose. When 3T6, SV3T3, and PY3T3 cells were exposed for as little as 2 min to 0.2 mMATP in buffered saline medium, the rate of efflux of the acid-soluble uridine (U) necleotide pool increased 20-30 times. In contrast, ATP had a much weaker effect (0- to 3-fold) on secondary cultures of mouse embryo fibroblasts, growing or resting 3T3 cells, and the human fibroblasts. The increase in permeability due to ATP was highly specific; guanosine TP, cytidine TP, UTP, ADP, inorganic phosphate, and various chelating agents all failed to show more than minimal effects when tested at 0.5 mM. The effect of ATP was pH-dependent and it occurred much faster at 37.5 C than at 20 C. Although the sensitization by ATP was temperature- dependent, the efflux itself proceeded as rapidly at 20 C as at 37.5 C. When the buffered saline medium was replaced with Dulbecco's modified Eagle's serum-free medium, the efflux was quickly suppressed. The presence of bicarbonate, divalent cations, and a more neutral pH all contributed to restore a normal permeability barrier. (35 refs.)

77-5394 **Metabolic Regulation of Steroidogenesis in Isolated Adrenocortical Carcinoma Cells. ACTH Regulation of Guanosine Cyclic 3':5'-Monophosphate Levels.** (Eng.) Perchellet, J. P. (Dept. Biochemistry, Univ. Tennessee, Center Health Sciences, Memphis, TN 38163); Sharma, R. K. *Biochem Biophys Res Commun* 78(2): 676-683; 1977.

The guanylate cyclase system in adrenocortical carcinoma cells was investigated and related to abnormal ACTH control as mediated by cyclic guanosine 3':5'-monophosphate (GMP). The lack of control of corticosterone synthesis may be due to an abnormal cyclic GMP-dependent protein kinase; however, no such enzyme has been isolated for these cells to date. (26 refs.)

77-5395 **Adenosine 3', 5'-Cyclic-Monophosphate Dependent Protein Kinase and Cyclic-AMP-Binding in Human Mammary Tumors.** (Eng.) Eppenberger, U. (Hormone Lab. and Experimental Endocrinology, Dept. Gynecology, Univ. Clinic Medical Sch., 4004 Basel, Switzerland); Talmadge, K.; Kung, W.; Bechtel, E.; Preisz, J.; Huber, P.; Jungmann, R. A.; Salokangas, A. *FEBS Lett* 80(1): 229-234; 1977.

In view of the experimental evidence implicating cyclic AMP (cAMP) and cAMP-dependent protein kinase in the regulation of gene transcription and cellular proliferation, cAMP-dependent and -independent protein kinase activities and cAMP binding activity in normal, dysplastic, and neoplastic human breast tissue were investigated. The specific enzyme activity (SA) of the cytosol cAMP-dependent protein kinase of primary carcinomas was 2.5-fold higher (227 picomoles of phosphate incorported/min/mg protein) than that of normal breast tissue (91). If the kinase activity is expressed on a per cell basis, however, there were significantly lower (by 2-3 times) cellular cAMP-dependent protein kinase levels in primary carcinoma tissue than in breast tissues with simple or proliferative dysplasia. A survey of substrate specifities revealed that the cytosal protein kinase from all samples preferred protamine, followed by total histone and histone F1. The primary tumors exhibited a two to threefold higher specific cAMP binding activity compared with normal tissue. Polyacrylamide gel electrophoresis resolved two cAMP-dependent protein kinase activities, PK-I(approx mol wt 213,000) and PK-II (approx mol wt 80,000), from the cytosol of both normal and neoplastic tissues. In addition, a slowly migrating form, PK-III, was detected in most neoplastic samles. The increased specific activities of cAMP-dependent nd -independent protein kinase and the increased cAMP inding can be correlated with progressive neoplastic dedifferentiation. (18 refs.)

77-5396 **Some Features of Cyclic Adenosine Monophosphate Metabolism in Mouse Liver and Hepatoma 22.** (Rus.) Solntseva, T. I. (Oncological Res. Center, USSR Acad. Medical Sciences, Moscow, USSR); Belousova, A. K. *Biokhimiia* 42(7): 1331-1337; 1977.

The levels of cyclic AMP (cAMP) and two forms of cAMP phosphodiesterase with low (PDE1) and high (PDE2) affinity for substrate were examined in mouse liver and transplanted hepatoma 22. A decrease in cAMP and an increase in the enzyme activity in the tumor cells suggested that the equilibrium between the two enzymatic forms is shifted towards PDE2 in tumor cells. (28 refs.)

77-5397 **Excretion of Corticosteroids and Catecholamines in Patients with Cancer of the Rectum and Stomach.** (Rus) Tarutinov, V. I. (Kiev Scientific Res. Inst. Roentgenology, Radiology and Oncology, Kiev, USSR); Maevskaia, L. P.; El'chits, T. V. *Vopr Onkol* 23(5): 45-50; 1977.

The excretion of 17-ketosteroids was reduced in patients with rectal and gastric cancer as was adrenal glucocorticoid function. Adrenaline and noradrenaline excretion was also low in gastrointestinal cancer patients. There was a distinct correlation between catecholamine and corticosteroid excretion in the urine. (25 refs.)

77-5398 **Phytosterols and Cholesterol in Malignant and Benign Breast Tumors.** (Eng.) Mellies, M. J. (Lipid Res. and General Clinical Res. Centers, Univ. Cincinnati, Coll. Medicine, Cincinnati, OH 45267); Ishikawa, T. T.; Glueck, C. J.; Crissman, J. D. *Cancer Res* 37(9): 3034-3036; 1977.

An examination was made of the sterol content of malignant and benign breast tumors and the hypothesis that malignant tumors have distinctive elevation of phytosterols. Of the 22 breast samples, 10 were from women with benign fibroadenoma or fibroystic disease, 8 were from women with breast carcinoma, and 4 were from normal breast tissue. Phytosterols were present in 9/10 benign and 7/8 malignant tumors and in 4/4 normal breast samples. Mean levels of tissue cholesterol, campesterol, stigmasterol, and β-sitosterol did not differ significantly among the samples of malignant and benign tumors and normal breast tissue. In the malignant tumors, tissue cholesterol correlated with campesterol and β-sitosterol, but not with stigmasterol. It is concluded that tissue phytosterol levels have little predictive specificity for malignant and nonmalignant breast lesions. It is also unlikely that there is any etiological relationship between phytosterols and breast carcinoma. (8 refs.)

77-5399 **The High Rate of Aerobic Glycolysis of Transformed 3T3 Cells Persists After Cell Homogenization.** (Eng.) Rozengurt, E. (Imperial Cancer Res. Fund Lab., Lincoln's Inn Fields, London W.C.2, England); Schneider, J. A.; Diamond, I.; Legg, A. *Biochem Biophys Res Commun* 78(1): 83-90; 1977.

Lactic acid production was increased 3.5- to 5-fold in confluent cultures of Simian virus 40- or polyoma virus-infected 3T3 cells as compared to noninfected cells. This high rate of glycolysis persisted after homogenization and centrifugation, and phosphofructokinase activity was also increased, indicating that differences in glycolytic activity do not depend critically on the cell membrane and may result from a change in the glycolytic pathway itself. (17 refs.)

77-5400 **Lipids of Cultured Hepatoma Cells: VIII. Utilization of D-(1-^{14}C) Glucose for Lipid Biosynthesis.** (Eng.) Welch, C. L. (Div. Gastroenterology, Dept. Medicine, Univ. Missouri Sch. Medicine, Columbia, MO 65201); Wood, R. *Lipids* 12(3): 245-253; 1977.

The utilization of glucose by minimal deviation hepatoma 7288C cells (HTC) for the biosynthesis of cellular lipids was investigated. HTC cells were incubated in serum-supplemented and serum-free Swim's 77 medium in the presence of D-(1-^{14}C) glucose (1.8 μCi/flask) for 1, 2, 4, 8, 12, and 24 hr. The percentage of D-(1-^{14}C) glucose oxidized to $^{14}CO_2$ and incorporated into cell matter and cell lipids was elevated in cells incubated in serum-free medium compared with serum-supplemented medium. The percentage distribution of total cell lipid radioactivity into individual neutral lipid classes from both serum-free and serum-supplemented cultures was as follows: sterols > triglycerides > free fatty acids > sterol esters. The percentage distriubtion of total cell lipid radioactivity into individual polar lipid classes of serum-supplemented cultures was as follows: phosphatidylcholine > phosphatidylinositol > sphingomyelin > phosphatidylethanolamine > phosphatidylserine. The distribution of glucose radiolabel into individual polar lipid classes of serum-free HTC cells was different from their serum-supplemented counterparts: sphingomyelin > phosphatidylcholine > phosphatidylinositol > phosphatidylethanolamine > phosphatidylserine. Glycerol from glyceride classes contained a high percentage of radioactivity than the acyl moieties, with this percentage being significantly elevated in serum-free cultures. These findings suggest the presence of other substrates, in addition to glucose, for HTC cell lipid synthesis; exogenous serum lipids appear to be the major contributors to HTC cell lipid mass. (32 refs.)

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